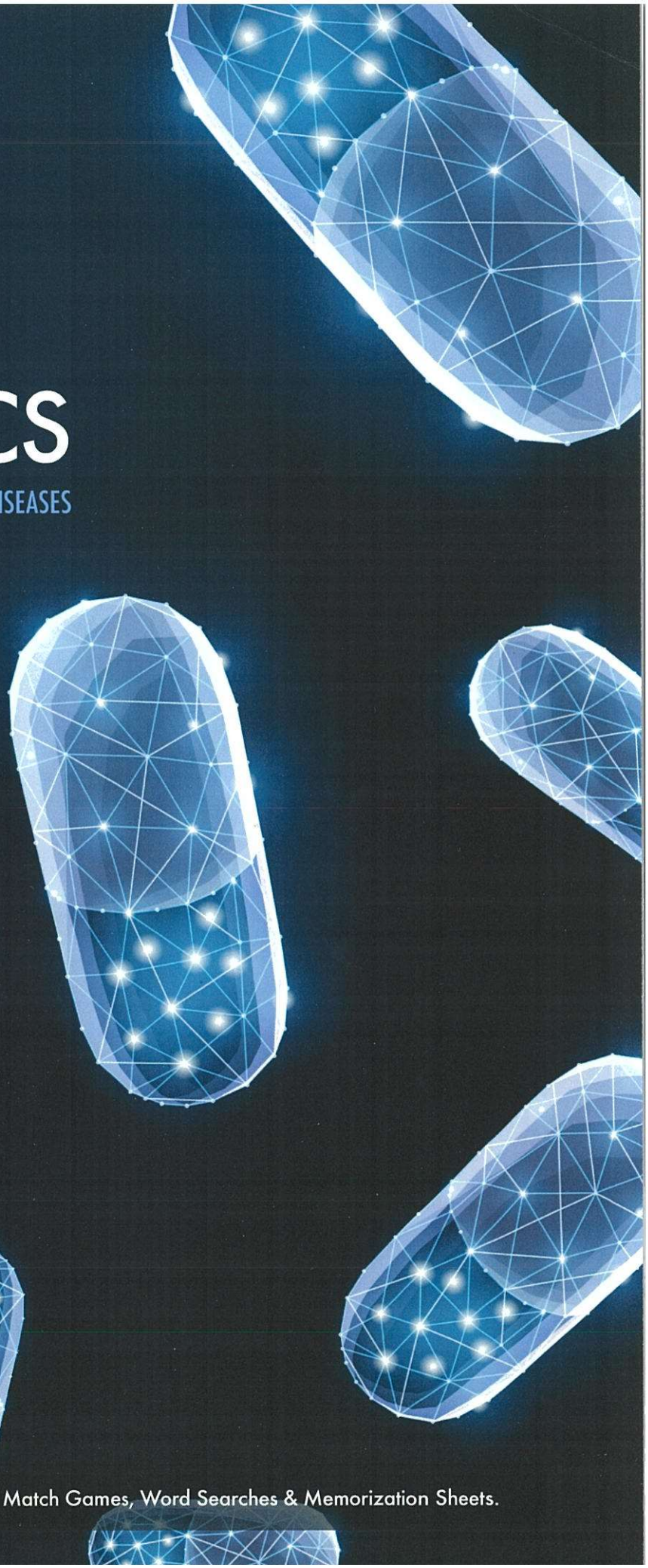
FIRST EDITION

LEARN ANTIBIOTICS

FOR ALL LEARNERS & TEACHERS OF INFECTIOUS DISEASES

A collection of resources for learning antimicrobial drugs from

IDSTEWARDSHIP



Resources Include: Cheat Sheets, Practice Tests, Match Games, Word Searches & Memorization Sheets.

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DEDICATION

This book is dedicated to the supporters of IDstewardship for without whom this would never be possible. It is also dedicated to my wife Alexandra for being amenable to me spending countless hours working on this passion project during evening and night hours. Finally, to my children Charlotte & Oliver for whom I hope they will have reasonable antibiotic options some day when they need them as adults.

DISCLAIMER

The information in this book is provided for study purposes only and is not intended to replace sound clinical judgement or be a substitute for a licensed healthcare practitioner's patient-specific medical advice. Infectious diseases are a complex study topic, certain content is simplified for teaching purposes.

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CONTENT DESCRIPTION

CHEAT SHEET: One-page summary study sheets

WORKSHEET: Tool for reviewing patient cases to apply a concept

MEMORIZATION SHEET: Use to practice identifying and recalling key information

WORD SEARCH: Puzzle game to support memorization of lists

MATCH GAME: Identify the item in the word bank that matches each description

RAPID FIRE TEST: Open-ended tests for recall challenge

QUICK FIRE TEST: Multiple choice test for identification practice

MASTER TEST: Multiple choice test with full answer explanations to reinforce concepts

TABLE OF CONTENTS

ITEM	PAGE
Take Notes	5-6
Antimicrobial Cheat Sheet	7
IV to PO Worksheet	8
Antibiotic Resistance Cheat Sheet	9
Antibiotic Resistance Memorization Sheet	10-11
MRSA Memorization Sheet	12-13
MRSA Drugs Word Search	14
Pseudomonas Drugs Word Search	15
Pseudomonas Memorization Sheet	16-17
Anaerobes Cheat Sheet	18
Clinical Microbiology Quick Fire Test	19-24
Core Spectra Rapid Fire Test	25-27
Mechanisms of Action Match Game I	28-29
Mechanisms of Action Match Game II	30-31
Mechanisms of Action Rapid Fire Test	32-35
Bugs & Drugs Cheat Sheet	36
Antibiotics Key Points Cheat Sheet	37
Drugs of Choice Memorization Sheet	38-39
Bugs & Drugs Master Test	40-56
Beta-Lactams Cheat Sheet	57
Beta-Lactam/Beta-Lactamase Inhibitor Cheat Sheet	58
Glycopeptides Cheat Sheet	59
Fluoroquinolones Cheat Sheet	60
Tetracyclines Cheat Sheet	61
Macrolides & Clindamycin Cheat Sheet	62
Pneumonia Cheat Sheet	63
Urinary Tract Infection Cheat Sheet	64
Malaria Cheat Sheet	65
Antimicrobial Toxicities Rapid Fire Test	66-69
Antifungals Memorization Sheet	70-71
Antifungals Cheat Sheet	72
Antifungal Drugs Rapid Fire Test	73-76
Antivirals Cheat Sheet	77
Biostatistics Cheat Sheet	78

STUDY NOTES

STUDY NOTES

Want more study material? Check out our online membership options!

SCAN ME

Antimicrobial Stewardship Cheat Sheet

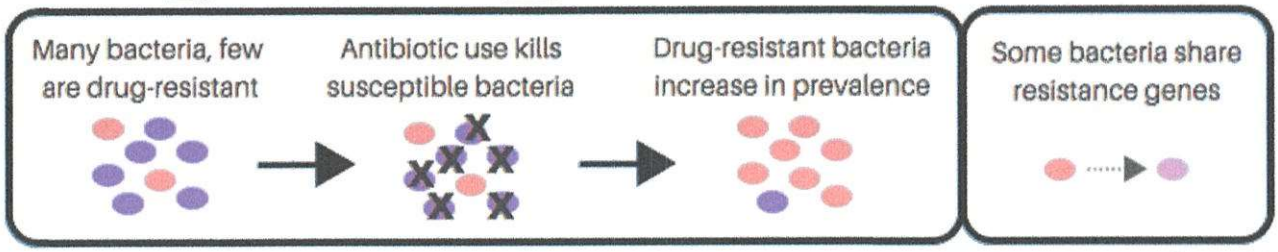
WHAT IS ANTIMICROBIAL STEWARDSHIP?

Antimicrobial = antibacterial, antiviral, antifungal, and antiparasitic drugs
Stewardship = managing use so it is appropriate and safe

- Antimicrobial stewardship goes beyond clinical infectious diseases; it includes elements of education, administration, quality assurance, regulatory compliance, systems optimization, infection control, microbiology, and more
- Antimicrobial stewardship is not about saving money, but good stewardship leads to reduced healthcare costs

WHY IS ANTIMICROBIAL STEWARDSHIP NEEDED?

The more we use antibiotics, the more we lose antibiotics. This is true whether or not the use is appropriate.


Many bacteria, few are drug-resistant
Antibiotic use kills susceptible bacteria
Drug-resistant bacteria increase in prevalence
Some bacteria share resistance genes

Reducing unnecessary (including inappropriate) antibiotic use = less drug-resistance + less chance for toxicity

HOW IS ANTIMICROBIAL STEWARDSHIP DONE?

Core Strategy #1: Prospective Audit with Intervention and Feedback

Cases are reviewed by antimicrobial stewardship program team members and feedback is given to providers in the form of interventions that are geared towards improving antimicrobial use practices

Core Strategy #2: Formulary Restriction

Retrospective: Provider can order and start medication, but requires approval to continue
Ex: Provider orders ertapenem on Monday afternoon, patient will get first dose Monday afternoon, but the provider will need approval by Tuesday afternoon to continue

Prospective: Provider cannot order medication without approval ahead of time
Ex: Providers orders ertapenem on Monday afternoon, but must gain approval prior to pharmacist processing it

Mixed: Provider must obtain approval ahead of time during certain hours, but not for others
Ex: If a provider orders ertapenem between 11 PM and 7 AM it gets reviewed retrospectively, but if it is ordered between 7:01 AM and 10:59 PM it is subject to prospective approval processes

Other Potential Interventions

IV to PO conversion	Renal dose adjustment	Streamlining therapy/Escalation
Penicillin skin testing	Dose optimization	Education
Pathways & guidelines	Point of care tests/ rapid diagnostics	Order forms

MONITORING ANTIMICROBIAL USE

Metric	How it is Done
Drug expenditures	Summarizes antimicrobial purchasing data
Defined Daily Dose (DDD)	Grams of drug stratified by "average" dose and adjusted by census
Days of Therapy (DOT)	Each day a patient receives one dose of that antibiotic is one DOT, adjust by census
Standardized Antimicrobial Administration Ratio (SAAR)	Compares observed to predicted DOTs

- Squeezing of the Balloon: when restricting the use of one drug leads to an increase in the use of another drug
- Defining "appropriate" can be a major challenge as many things within infectious diseases are not "black and white"
- Antimicrobial stewardship is a team sport that requ ires involvement from a variety of healthcare professionals including: physicians, pharmacists, nurses, micro lab staff, administrators, quality officers, patients, caregivers, and others
- Some excellent antimicrobial stewardship resources include: IDSA guidelines and the CDC Core Elements

IV to PO Worksheet

★★★★★ BEFORE COMPLETING, MAKE SURE ANTIBIOTICS ARE NEEDED ★★★★★

...and remember: *The bug does not know how the drug gets there!...* So: *If the gut works, use it!*

ALLERGIES: □ NKDA □ penicillin □ sulfa □ Other/details:_____ **DIET ORDER:** _____

INFECTION TYPE: _____

MICROBIOLOGY DATA/ TARGET ORGANISMS: _____

MEDICATIONS:

Days of therapy so far: ____days (usually 24-48 hrs required prior to IV→PO to allow for defervescence)

- Abx history: _____
- Relevant *inpatient* medications: _____
- Relevant *outpatient* medications: _____

Factor	Yes	No	Notes/ Comments
Worsening infection-related signs/ symptoms? (e.g., pain, erythema)	□	□	
Mental status issues?	□	□	
Abnormal heart rate? (e.g., > 90 bpm)	□	□	
Abnormal respiratory rate? (e.g., < 20 bpm)	□	□	
Abnormal blood pressure / MAP?	□	□	
Abnormal or worsening body temperature? (e.g., >100.4 F in last 24 hrs?)	□	□	
Antipyretic use?	□	□	
Abnormal or worsening WBC?	□	□	
Renal dysfunction?	□	□	
Hepatic dysfunction?	□	□	
Patient having nausea/vomiting?	□	□	
Patient having trouble swallowing?	□	□	
Using NG / PEG / PEJ tube for meds?	□	□	
Patient on PPN or TPN?	□	□	
No other oral medications?	□	□	
History of non-compliance?	□	□	
Active gastric bleed	□	□	
Gastrointestinal obstruction (e.g., ileus)	□	□	
Receiving high-dose vasopressors	□	□	
Problematic social/ behavioral issues	□	□	

Oral Bioavailability*

(*may vary due to dosage, DDIs, DFIs, formulation, fasting or not, patient-specific variables, or other)

<50%	50-75%	>75%
Acyclovir (15%), Amoxicillin-clavulanic acid (30%), Azithromycin (40%), Cefixime (45%), Cefuroxime axetil (40%), Letermovir (35%)	Amoxicillin (75%), Ampicillin (50%), Cefpodoxime proxetil (50%), Delafloxacin (60%), Dicloxacillin (70%), Valacyclovir (55%), Valganciclovir (60%)	Ceftibuten (80%), Ciprofloxacin (80%), Clindamycin HCl (90%), Doxycycline (>90%), Fluconazole (>90%), Isavuconazonium sulfate (95%), Levofloxacin (100%), Linezolid (100%), Metronidazole (90%), Minocycline HCl (90%), Moxifloxacin (90%), Rifampin (90%), SMX-TMP (95%), Tedizolid (90%), Voriconazole (95%)

Abbreviations: abx = antibiotics, bpm = beats or breaths per minute, DDI = drug-drug interaction, DFI = drug-food interaction, MAP = mean arterial pressure, NG = nasogastric, NKDA = no known drug allergies, PEG = percutaneous endoscopic gastrostomy, PEJ = percutaneous endoscopic jejunostomy, PPN = peripheral parenteral nutrition, TPN = total parenteral nutrition, WBC = white blood cell

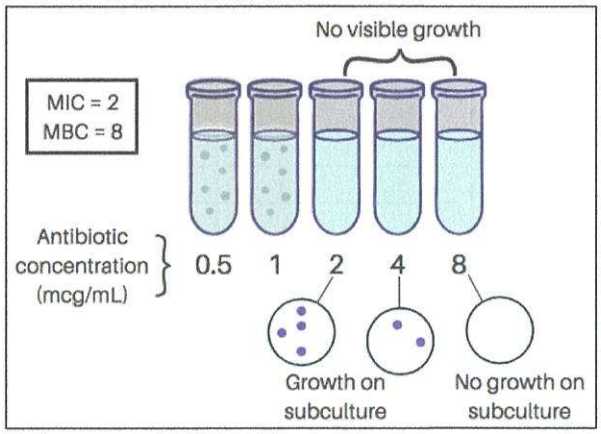
Disclaimer: Factors not listed on this worksheet may impact IV to PO transition decisions.

Antibiotic Resistance Cheat Sheet

Antimicrobial resistance is incredibly complex. This cheat sheet is intended to be a quick study reference and is not a comprehensive resource for clinical decision making.

Definitions (Generalization)	
Pan drug-sensitive (aka pan-sensitive)	An organism sensitive to all drugs typically tested for potential treatment
Multidrug-resistant (MDR)	An organism resistant to a few drug classes typically used for treatment
Extensively drug-resistant (XDR)	An organism resistant to most drug classes typically used for treatment
Pan drug-resistant (PDR)	An organism resistant to all drug classes typically used for treatment
Minimum inhibitory concentration (MIC)	The lowest antibiotic concentration to inhibit visible bacterial growth
Minimum bactericidal concentration (MBC)	The lowest antibiotic concentration to kill a bacteria
Breakpoint	MIC cutoff points for differentiating an organism as S, I, or R
Sensitive (S)	An organism with an MIC at or below the assigned breakpoint for S
Intermediate (I)	An organism with an MIC that falls between the breakpoint for S and R
Resistant (R)	An organism with an MIC that is above the breakpoint for S or I

- The lowest MIC does not necessarily indicate the best drug to select for an infection and thus MICs are not always reported
- MIC testing can be done in several ways, the method pictured on the right is called broth dilution
- Molecular-based tests for antimicrobial resistance such as PCR, PNA-FISH, MALDI-TOF, and microplex multiarray provide more rapid results than traditional sensitivity testing and are revolutionizing the field of clinical microbiology by enabling faster decision making
- Breakpoints are defined by organizations such as CLSI and EUCAST Breakpoints can change as guidelines are updated
- Breakpoints may vary by site of infection (*e.g.,* urine versus blood)
- Breakpoints are specific to each bacteria-antibiotic combination
- When the lab reports a list of antibiotics for which a bacteria is S, I, or R, that is called an antibiogram



Antimicrobial resistance can be intrinsic/inducible (*e.g.*, chromosomal) or acquired (*e.g.*, via plasmids)
The 4 main mechanisms of microbial resistance that can be present are:

1. **Change in the binding site**: changes at the site of action confer bacterial resistance (*i.e.*, the lock to the safe changes)
2. **Enzymatic degradation**: enzymes that hydrolyze antibiotics, disrupting their structure and rendering them inactive
3. **Porin channels**: loss of porin channels confers reduced ability for antibiotics to penetrate into the microbe
4. **Efflux pumps**: increased efflux pump activity reduces the concentration of antibiotic inside the bacterial cell

Bonus: *Staphylococcus aureus* can have increasing MICs to glycopeptides like vancomycin via thickening of the cell wall

Some Important Resistance Genes		
Gene / Protein/ Enzyme	**Resistance Type**	**Notes**
MecA	Binding site change	PBP2 changes to PBP2a → MSSA into MRSA
VanA, VanB, VanC	Binding site change	Leads to vancomycin resistance in Enterococci
gyrA, gyrB, parC	Binding site change	Can cause fluoroquinolone resistance
Erm	Binding site change	Can cause plasmid-mediated resistance in clindamycin & macrolides
TetA, TetB, TetC	Efflux pump	Can make *E. coli* resistant to tetracyclines
OprD	Porin channel	Can make *Pseudomonas aeruginosa* resistant to carbapenems
KPC, CTX-M, TEM, SHV	Enzymatic	Ambler class A
NDM, VIM, IMP	Enzymatic	Ambler class B, zinc-dependent metallo-beta-lactamases
AmpC	Enzymatic	Ambler class C, inducible-type resistance
OXA	Enzymatic	Ambler class D

- The Ambler classification is used to differentiate β-lactamases that hydrolyze β-lactam antibiotics
- HECK-YES has been used as an acronym for organisms with potential for inducible AmpC-mediated resistance and includes ***H**afnia alvei*, ***E**nterobacter cloacae*, ***C**itrobacter freundii*, ***K**lebsiella aerogenes*, and ***Yers**inia enterocolitica*

Antibiotic Resistance Memorization Sheet

Antibiotic Resistance Challenge!

A _____ (MIC) is the _____ concentration that will _____ _____ bacterial growth.

MIC cut points for differentiating an organism as _____ (S), _____ (I), or _____ (R) are called _____.

MIC breakpoints can vary depending on both the _____ and _____.

The lowest MIC _____ indicate the best drug to treat the bug.

An organism that is susceptible or resistant to all drugs it is tested against is called _____ or _____, respectively.

At the most fundamental level, antimicrobial resistance can either be _____ (*i.e.*, _____) or _____ (*e.g.*, via _____).

The four major antibiotic resistance mechanisms are:

(1) _____
(2) _____
(3) _____
(4) _____

The _____ gene causes MSSA to turn into MRSA, which is example of the _____ type of resistance.

→ In this example _____ turns into _____ (_____ → _____)

The _____, _____,and _____ genes cause Enterococcus to become resistant to vancomycin, which is example of the _____ type of antibiotic resistance.

→ In this example _____ turns into _____.

The _____, _____, and _____ genes can cause resistance to fluoroquinolones and are an example of _____.

The _____ gene that can make *Pseudomonas aeruginosa* resistant to carbapenems is mediated by _____.

The _____, _____, and _____ genes can make *E. coli* resistant to tetracyclines and is mediated by _____.

Beta-lactamase enzymes that hydrolyze penicillins are called _____ and enzymes that hydrolyze cephalosporins are called _____.

The Ambler classification is used to differentiate _____, match the Ambler class to the enzyme…

KPC = _____	Oxa = _____	AmpC = _____
CTX-M = _____	VIM = _____	SHV = _____
IMP = _____	NDM = _____	TEM = _____

Even though KPC stands for _____, non-Klebsiella species can be _____ producers.

_____ bacteria (especially _____) are notorious for exhibiting _____ at once.

A _____ test is a simple phenotypic test that can detect the presence of _____ in bacteria.

_____ can be used to identify specific resistance genes and for organism identification.

ANSWERS

Antibiotic Resistance Challenge!

A _*minimum inhibitory concentration*_ (MIC) is the _*lowest*_ concentration that will _*inhibit*_ _*visible*_ bacterial growth.

MIC cut points for differentiating an organism as _*susceptible*_ (S), _*intermediate*_ (I), or _*resistant*_ (R) are called _*breakpoints*_.

MIC breakpoints can vary depending on both the _*organism*_ and _*antimicrobial agent*_.

The lowest MIC _*does not necessarily*_ indicate the best drug to treat the bug.

An organism that is susceptible or resistant to all drugs it is tested against is called _*pan-susceptible*_ or _*pan-resistant*_, respectively.

At the most fundamental level, antimicrobial resistance can either be _*inducible/intrinsic*_ (*i.e.*, _*chromosomal-mediated*_) or _*acquired*_ (*e.g.*, via _*plasmid-mediated*_).

The four major antibiotic resistance mechanisms are:

(1) _*altered drug binding*__
(2) _*production of enzymes that hydrolyze antibiotics*_
(3) _*porin channel modifications*_
(4) _*increased efflux pump activity*_

The _*MecA*_ gene causes MSSA to turn into MRSA, which is example of the _*altered binding site*_ type of resistance.

→ In this example _*penicillin binding protein 2*_ turns into _ *penicillin binding protein 2a*_ (_*PBP2*_ → _*PBP2a*_).

The _*VanA*_, _*VanB*_,and _*VanC*_ genes cause Enterococcus to become resistant to vancomycin, which is example of the _*altered drug binding*_ type of antibiotic resistance.

→ In this example _*D-ala, D-ala*_ turns into _*D-ala, D-lac*_.

The _*gyrA*_, _*gyrB*_, and _*parC*_ genes can cause resistance to fluoroquinolones and are an example of _*altered drug binding*_.

The _*OprD*_ gene that can make *Pseudomonas aeruginosa* resistant to carbapenems is mediated by __*porin channel modifications*__.

The _*TetA*_, _*TetB*_, and _*TetC*_ genes can make *E. coli* resistant to tetracyclines and is mediated by _*increased efflux pump activity*_.

Beta-lactamase enzymes that hydrolyze penicillins are called _*penicillinases*_ and enzymes that hydrolyze cephalosporins are called _*cephalosporinases*_.

The Ambler classification is used to differentiate _*Ambler Class*_, match the Ambler class to the enzyme…

KPC = _*Class A*_	Oxa = _*Class D*_	AmpC = _*Class C*_
CTX-M = _*Class A*_	VIM = _*Class B*_	SHV = _*Class A*_
IMP = _*Class B*_	NDM = _*Class B*_	TEM = _*Class A*_

Even though KPC stands for _*Klebsiella pneumoniae carbapenemase*_, non-Klebsiella species can be _KPC_ producers.

*Gram negative* bacteria (especially _*Pseudomonas aeruginosa*_) are notorious for exhibiting __*multiple different resistance mechanisms*_ at once.

A _*modified Hodge*_ test is a simple phenotypic test that can detect the presence of _*carbapenemase enzymes*_ in bacteria

*Rapid molecular diagnostic tests* can be used to identify specific resistance genes and for organism identification.

MRSA Memorization Sheet

MRSA & Microbiology

MRSA is a Gram _____ _____ that grows in _____ (or _____). It looks like _____ under a microscope.

MRSA is catalase-_____ and coagulase-_____.

MSSA turns into MRSA when the _____ gene is present, which changes _____ to _____.

When MRSA has a vancomycin MIC of ___ mcg/mL or higher, consider avoiding vancomycin and beware increased _____ MICs to the MRSA isolate.

A D-Test can be used to confirm *Staphylococcus aureus* sensitivity to _____.

A MRSA _____ has a high _____ for MRSA pneumonia and can be used to stop empiric _____ for most scenarios.

Drugs with MRSA Activity

Glycopeptides:1. _____ 2. _____ (_____) 3. _____ (_____)

4. _____ (_____) 5. _____ (_____)

Sulfas: 1. _____-_____ (_____, _____)

Cephalosporins: 1. _____ (_____)

Lincosamides: 1. _____ (_____)

Tetracyclines: 1. _____ 2. _____ (_____) 3. _____ (_____)

4. _____ (_____) 5. _____ (_____) 6. _____ (_____)

Oxazolidinones: 1. _____ (_____) 2. _____ (_____)

Fluoroquinolones: 1. _____ (_____)

→ Other fluoroquinolones may have activity, but should not be used routinely _____for MRSA.

Other: 1. _____ (_____) 2. _____ (_____)

3. _____ (_____) 4. _____ (_____)

→ _____ should not be used monotherapy for MRSA infection

→ _____ is only for UTI suppression (not for treatment)

→ _____ and _____ are for lower UTI only

→ _____/ _____ (_____) is rarely used in clinical practice; hence it really is not worth memorizing even though it can cover MRSA

ANSWERS

MRSA & Microbiology

MRSA is a Gram _positive_ _cocci_ that grows in _clusters_ (or _tetrads_). It looks like _grapes_ under a microscope.

MRSA is catalase-_positive_ and coagulase-_positive_.

MSSA turns into MRSA when the _MecA_ gene is present, which changes __PBP2_ to _PBP2a_.

When MRSA has a vancomycin MIC of _2_ mcg/mL or higher, consider avoiding vancomycin and beware increased _daptomycin_ MICs to the MRSA isolate.

A D-Test can be used to confirm *Staphylococcus aureus* sensitivity to _clindamycin_.

A MRSA _nasal swab_ has a high _negative predictive value_ for MRSA pneumonia and can be used to stop empiric _vancomycin_ most times when it is prescribed empirically for a respiratory tract infection.

Drugs with MRSA Activity

Glycopeptides:1. _Vancomycin_ 2. _Daptomycin_ (_Cubicin_) 3. _Telavancin_ (_Vibativ_)

4. _Oritavancin_ (_Orbactiv, Kimyrsa_) 5. _Dalbavancin_ (_Dalvance_)

fas: 1. _Sulfamethoxazole_-_Trimethoprim_ (_Bactrim_, _Septra_)

Cephalosporins: 1. _Ceftaroline_ (_Teflaro_)

Lincosamides: 1. _Clindamycin_ (_Cleocin_)

Tetracyclines: 1. _Tetracycline_ 2. _Minocycline_ (_Minocin_) 3. _Doxycycline_ (_Doryx_)

4. _Tigecycline_ (_Tygacil_) 5. _Eravacycline_ (_Xerava_) 6. _Omadacycline_ (_Nuzyra_)

Oxazolidinones: 1. _Linezolid_ (_Zyvox_) 2. _Tedizolid_ (_Sivextro_)

Fluoroquinolones: 1. _Delafloxacin_ (_Baxdela_)
→ Other fluoroquinolones may have activity, but should not be used routinely _as monotherapy_for MRSA.

Other: 1. _Rifampin_ (_Rifadin) _ 2. _Methenamine (_Hiprex, Urex_)_

3. _Nitrofurantoin_ (_Macrobid, Macrodantin_) 4. _Fosfomycin_ (_Monurol_)

→ _Rifampin_ should not be used monotherapy for MRSA infection

→ _Methenamine_ is only for UTI suppression (not for treatment)

→ _Nitrofurantoin_ and _Fosfomycin_ are for lower UTI only

→ _Quinupristin_/ _Dalfopristin_ (_Synercid_) *is* rarely used in clinical practice; hence it really is not worth memorizing even ugh it can cover MRSA

MRSA Drugs Word Search

A G C E N L E T T I J X D N H A T S O A B Y R W I
N D M O Z T I O T F D Y Z Y E P J E H T S T K D E
R E T B L F I A R S E P T R A V C M F I T S Z A V
H L S E X U K L H D G V B J L Y U W X L X E D L A
C A P W F X D C X U O C A Y L A I B S T A T U V S
U F A P A V A N C O M Y C I N G T Y R Y O R B A H
B L D D B I P E S H A B T L N K E O G W E C O N O
I O O A A N T D B A D E R X R O L E R G Z Y S C X
C X L F X V O Q L G A A I J C I A N E B U E S E E
I A X F D T M Y C Z C R M O U C V H R V A N X Y R
N C S C E N Y X R X Y R I T Z I A V A A C C I E A
T I U G L B C A A N C D D O O N N V V I B A T I V
L N M G A I I T B Z L I N E T H C G A X O O Y I A
D X P K T X N D T P I K S S D D I N C E L H L N V
F A O P I J A D Z X N P I B P A N M Y L B A I G T
A V N B T X R O A R E M M L Q P Q L C M B O N B Y
M C Z V M Y C I N M O G M Y G M E S L G A X E F B
Z R N E A K H C B M Y I F E U A S L I S Y N O L F
L I N E Z O L I D B G C G M E A E C N P A R Q H A
I F L R B R X S A O F L I I J R V Y E A P C U K N
N A R W D S J H Q Z V E X N O Y C I N Y I E M Y T
S M Y F V C V K M E W O E O R I F A D I N F A F N
B P R Y E L A I C L P C Z C T N C A R H P T R A R
R I E Y T O O Z T T H I V I X T X M R R D A N Y N
A N T I G E C Y C L I N E N U Z Y R A L E R H R U
K V D D A L B A V A N C I N H Z W I R O Y O R D T
E I W X H S X U A G N D P P Z K Z J E Z A L G D A
D C Z V U V E Z M Y E P I V S V T H R E Y I X G T
O X Z Y C L S C A G Y W I E V I O E C U X N D W E
O T I T V K S H M J P R B R J A V X H M N E R G D
Y A G G K O T O U X D B E O V A K E A X L C D T I
E S Q D D O X Y C Y C L I N E T Y F X C V Y G I Z
K S Y F E A P S U L I N E T Z T A N A T L C Z E O
V E A Y L D Z A G Z C Q C H P W U P P E R Y V K L
T O P B O M I N O R I T A V A N C I N G B O B S I
M I N O C Y C L I N E B E U P R X N W T A R R E D

Word Bank of Drugs that cover MRSA

These brand and generic drug names can be found above either vertical, horizontal, or diagonal.

Bactrim
Baxdela
Ceftaroline
Clindamycin
Cleocin
Cubicin
Dalbavancin
Dalvance
Daptomycin
Delafloxacin
Doxycycline
Eravacycline
Linezolid
Minocin
Minocycline
Nuzyra
Omadacycline
Orbactiv
Oritavancin
Rifampin
Rifadin
Septra
Sivextro
Tedizolid
Teflaro
Telavancin
Tigecycline
Vancomycin
Vibativ
Xerava
Zyvox

Pseudomonas Drugs Word Search

P O L Y M Y X I N B A D T R L O U T B S B M O K E
O P R I M A X I N P C R M P D F C A A R M G P V L
L C I T A N B C E F I D E R O C O L X C A P C Y S
Y M M P H F T J N F P L M Y R E Z X D N X D E C F
M L I C E O H A K U R R E R I F E F E I I G F H S
Y W P U F R E A H P O N C O P E X E L G P F T K M
X U E A R T A R A W L M V X E P Z T A H I R O E D
I H N M N A E C M Z J A H A N I D R S I M E L V D
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A T T Z M N N I N B K E U L D Z B X O T V P Z E L
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M F E C O R X U T V F A D R H B E B F A W S E A V
K L B I B I Z O S Y N T Z U G I G R R M X H Y Q O
S O A V J R E S H C G I T O B R A Y C I N K F U C
L X C N O A V Z F A Z N A T X S L J M T O B C I T
C A T E B N B A R Z H G J Z S B C T A C T A O X R
Y C A M W R L D V U P N C J T L E H I J M X L T I
H I M E R O P E N E M V A B O R B A C T A M I P F
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G E N T A M I C I N R B B H S Q U O F V B N T W D
M A P X M T O B R A M Y C I N U U N N Z B D I O I
E S V Y G O Z P D E Y L E V O F L O X A C I N J N
T C Z A C B A Y U R S P U G D J T S Y R M R V A P
C E F T A Z I D I M E A V I B A C T A M A S B S N

Word Bank of Drugs that can cover *Pseudomonas aeruginosa*

These brand and generic drug names can be found above either vertical, horizontal, or diagonal.

Amikacin
Avycaz
Azactam
Aztreonam
Baxdela
Cefepime
Cefiderocol
Ceftazidime
Ceftazidime-avibactam
Ceftolozane-tazobactam
Cipro
Ciprofloxacin
Colistin
Delafloxacin
Doribax
Doripenem
Fetroja
Fortaz
Gentamicin
Imipenem-cilastatin
Imipenem-cilastatin-relebactam
Levaquin
Levofloxacin
Maxipime
Meropenem
Meropenem-vaborbactam
Merrem
Piperacillin-tazobactam
Plazomicin
Polymyxin B
Polymyxin E
Primaxin
Recarbrio
Rifadin
Rifampin
Tobramycin
Vabomere
Zemdri
Zerbaxa
Zosyn

Pseudomonas Memorization Sheet

Pseudomonas aeruginosa & Microbiology

Pseudomonas aeruginosa is a ___-_____ Gram _____ _____ (_____).

Pseudomonas stains _____ upon Gram stain.

Pseudomonas aeruginosa is oxidase _____ and catalase _____.

Pseudomonas aeruginosa can become resistant to antimicrobial drugs via increased _____ activity, _____ modifications, or by producing _____ that hydrolyze antibiotics.

Drugs with activity versus *Pseudomonas aeruginosa*

Penicillins: 1. _____ (_____) 2. _____ (_____)

Cephalosporins: 1. _____ (_____) 2. _____ (_____)

3. _____ (_____) 4. _____ (_____)

Carbapenems: 1. _____ (_____) 2. _____ (_____)

3. _____ (_____) 4. _____ (_____)

5. _____ (_____)

Monobactam: 1. _____ (_____)

Aminoglycoside: 1. _____ 2. _____

3. _____ 4. _____ (_____)

Polymyxins: 1. _____ (_____) 2. _____

Fluoroquinolones: 1. _____ (_____) 2. _____ (_____)

3. _____ (_____)

Other: 1. _____ (_____) 2. _____ (_____)

→ _____ should not be used _____ for Pseudomonas infection

→ _____ is only for _____ (not for _____)

Inhaled drugs with anti-Pseudomonal activity: 1. _____ (_____) 2. _____ (_____)

3. _____ (_____) 4. _____ (_____)

Piperacillin-tazobactam versus cefepime: Both have _____ activity. _____ has activity versus _____and _____ while _____ does not.

Some important drugs that notably <u>do not</u> cover *Pseudomonas*:

1. _____ (_____) 2. _____ (_____)

3. _____ (_____) 4. _____ (_____) 5. _____ (_____)

ANSWERS

Pseudomonas aeruginosa & Microbiology

Pseudomonas aeruginosa is a _non_-_fermenting_ Gram _negative_ _rod_ (_bacilli_).

Pseudomonas stains _pink/red_ upon Gram stain.

Pseudomonas aeruginosa is oxidase _positive_ and catalase _positive_.

Pseudomonas aeruginosa can become resistant to antimicrobial drugs via increased _efflux pump_ activity, _porin channel_ modifications, or by producing _enzymes_ that hydrolyze antibiotics.

Drugs with activity versus *Pseudomonas aeruginosa*

Penicillins: 1. _piperacillin-tazobactam_ (_Zosyn_) 2. _Ticarcillin-clavulanic acid_ (_Timentin_)

Cephalosporins: 1. _Ceftazidime_ (_Fortaz, Tazicef_) 2. _Cefepime_ (_Maxipime_)

3. _Ceftolozane-tazobactam_ (_Zerbaxa_) 4. _Ceftazidime-avibactam_ (_Avycaz_)

Carbapenems: 1. _Meropenem_ (_Merrem_) 2. _Doripenem_ (_Doribax_)

3. _Imipenem-cilastatin_ (_Primaxin_) 4. _Meropenem-Vaborbactam_ (_Vabomere_)

5. _Imipenem-cilastatin-relebactam_ (_Recarbrio_)

Monobactam: 1. _Aztreonam_ (_Azactam_)

Aminoglycoside: 1. _Tobramycin_ 2. _Gentamicin_

3. _Amikacin_ 4. _Plazomicin_ (_Zemdri_)

Polymyxins: 1. _Polymyxin E_ (_Colistin_) 2. _Polymyxin B_

Fluoroquinolones: 1. _Ciprofloxacin_ (_Cipro_) 2. _Levofloxacin_ (_Levaquin_)

3. _Delafloxacin_ (_Baxdela_)

Other: 1. _Rifampin_ (_Rifadin_) 2. _Methenamine_ (_Urex, Hiprex_)

→ _Rifampin_ should not be used _monotherapy_ for Pseudomonas infection

→ _Methenamine_ is only for _UTI suppression_ (not for _treatment_)

Inhaled drugs with anti-Pseudomonal activity: 1. _Tobramycin_ (_TOBI_) 2. _Aztreonam_ (_Cayston_)

3. _Polymyxin E_ (_Colistin_) 4. _Amikacin_ (_Arikayce_)

Piperacillin-tazobactam versus cefepime: Both have _anti-pseudomonal _ activity. _Piperacillin-tazobactam_ has activity versus _anaerobes_ and _Enterococci_ while _cefepime_ does not.

Some important drugs that notably <u>do not</u> cover *Pseudomonas*:

1. _Ampicillin-sulbactam_ (_Unasyn_) 2. _Ceftriaxone_ (_Rocephin_)

3. _Ertapenem_ (_Invanz_) 4. _Tigecycline_ (_Tygacil_) 5. _Moxifloxacin_ (_Avelox_)

Anaerobes Cheat Sheet

Anaerobic Bacteria: bacteria that do not live or grow when oxygen is present. Obligate anaerobes only grow in the absence of oxygen. Facultative anaerobes are able to grow with or without free oxygen.

Clinically Notable Anaerobic Bacteria			
Organism name	**Gram Stain**	**Go-To Drug(s)**	**Notes**
Clostridium perfringens	Gram + rod	Penicillin G	Known as "gas gangrene"; can cause a severe necrotizing infection called clostridial myonecrosis
Clostridium tetani	Gram + rod	See CDC guidance, more than antibiotics	Causes tetanus disease; has a vaccine; tetanus IG and supportive care important for treatment
Clostridium difficile	Gram + rod	Vancomycin PO, fidaxomicin	Spores are not killed by hand sanitizer *C. diff* disease can be caused by antibiotic use
Peptostreptococcus spp.	Gram + cocci	Penicillin G, Amoxicillin	Associated with mouth infections & skin infections
Cutibacterium acnes	Gram + rod	Penicillin G	Formerly known as *Propionobacterium acnes*; implicated for causing acne vulgaris
Prevotella spp. *Fusobacterium* spp.	Gram – rods	Metronidazole, Clindamycin, Amox/clav	Associated with bite wounds and oral infections
Eikenella corredens	Gram – rod	Amox/clav	Associated with bite wounds; beware resistance to metronidazole and clindamycin
Bacteroides fragilis	Gram – rod	Metronidazole	Associated with intra-abdominal infections

Comparison of Select Anti-Anaerobic Drugs					
	Clindamycin	**Metronidazole**	**Amoxicillin/ clavulanic acid**	**Cefoxitin**	**Moxifloxacin**
Brand name:	Cleocin	Flagyl	Augmentin	Mefoxin	Avelox
Class:	Lincosamide	Nitroimidazole	β-lactam/ β-lactamase inhibitor	Cephalosporin (cephamycin)	Fluoroquinolone
Mechanism:	Binds to 50S ribosomal subunit, interfering with protein synthesis	Interrupts DNA helix, inhibits protein synthesis	Interferes with bacterial cell wall synthesis	Interferes with bacterial cell wall synthesis	Interferes with topoisomerase & DNA gyrase
Available IV & PO:	Yes	Yes	No*	No	Yes
Typical adult dose:	600-1,800 mg/day in 2-4 divided doses	500mg Q8H	500-875mg Q12H	1-2gm Q6-8H	400mg Q24H
Renal adjust:	No	No	CrCl < 30	CrCl < 50	No
B. frag. coverage:	Poor	Good	+/-	+/-	Poor
Side effects:	Diarrhea	Metallic taste, peripheral neuropathy (more w/ frequent use)	Diarrhea, hypersensitivity	Diarrhea, hypersensitivity	Many, see fluoroquinolone cheat sheet
Notes:	Has MRSA activity, but beware clindamycin resistance in MRSA	No longer first-line for *C. difficile* infxn	Pip/taz has better *B. frag.* coverage than amox/clav	Common intra-abdominal surg. prophylaxis drug	Not commonly a first-line agent

*Amoxicillin-clavulanic acid is available IV in some countries, but not in the United States. In the United States, ampicillin-sulbactam (Unasyn) serves as the IV counterpart to oral amoxicillin-clavulanic acid

-*NOTE 1*: Beyond the cephamycins (cefoxitin and cefotetan), anaerobic activity of cephalosporins is negligible

-*NOTE 2*: Penicillin, ampicillin, piperacillin-tazobactam, carbapenems, tigecycline, eravacycline, and omadacycline all also have considerable anti-anaerobic coverage. Fidaxomicin is only for *C. difficile* infection, it is in the macrolide class.

- Susceptibility testing is not usually done for anaerobes due to inadequate lab techniques and poor-quality controls
- For human/animal bite wounds, amoxicillin-clavulanic acid is a go-to, providing good oral aerobic and anaerobic coverage
- Some say 'clindamycin above the diaphragm, metronidazole below the diaphragm' → b/c below the diaphragm *B. fragilis* coverage is not likely needed and clindamycin covers most of the orodental flora
- Clinicians may suspect anaerobes in a wound if a bad smell is present (*e.g.*, common in diabetic foot infxn)

***C. difficile* Key Points**
- Do not test formed stool for *C. difficile*
- Rule-out other causes of diarrhea to make dx
- Do not test for cure at EOT
- Bezlotoxumab only indicated for adjunctive therapy

Select Abbreviations: CrCl = creatinine clearance, dx = diagnosis, EOT = end of therapy, IG = immune globulin, infxn = infection

Clinical Microbiology Quick Fire Test

Question #1
What is the definition of a minimum inhibitory concentration (MIC)?
A. The lowest drug concentration that will kill a bacteria after overnight incubation
B. The lowest drug concentration that will inhibit visual bacterial growth after overnight incubation
C. The highest drug concentration that will kill a bacteria after overnight incubation
D. The highest drug concentration that will inhibit visual bacterial growth after overnight incubation

Question #2
Which of the following best describes MIC breakpoints?
A. Discriminatory concentrations used to identify which microbiology susceptibility tests should be performed
B. Discriminatory concentrations used to interpret whether a bacteria should be labeled as susceptible, intermediate, or resistant
C. Numeric values that identify when microbiology lab equipment will malfunction
D. Numeric values that identify how rapid a bacteria can grow

Question #3
The MIC breakpoints for vancomycin and MRSA are:
$\leq$ 2 mcg/mL = susceptible
4-8 mcg/mL = intermediate
> 16 mcg/mL = resistant
If an MIC for vancomycin is found to be 2 mcg/mL, according to these breakpoints how should the microbiology lab report the result?
A. Susceptible
B. Intermediate
C. Resistant
D. Invalid

Question #4
A microbiologist does two Gram stains. The first for a Gram positive bacteria and the second for a Gram negative bacteria. What can we expect the color of the Gram stains to be?
A. First = Purple, Second = Purple
B. First = Purple, Second = Pink
C. First = Pink, Second = Purple
D. First = Pink, Second = Pink

Question #5
Which of the following is not considered a molecular rapid diagnostic test?
A. PCR (polymerase chain reaction)
B. PNA FISH (peptide nucleic acid fluorescence in situ hybridization)
C. BMD (broth microdilution)
D. MALDI-TOF (matrix-assisted laser desperation ionization time-of-flight spectrometry)

Question #6
The laboratory reports an organism as a Gram positive cocci in clusters. Which one of the following could this result be?
A. *E. coli*
B. *Streptococcus pyogenes*
C. *Staphylococcus aureus*
D. *Listeria monocytogenes*

Question #7
The laboratory reports an organism is Gram positive cocci in clusters and coagulase positive. Which of the following is this?
A. *Staphylococcus epidermidis*
B. *Staphylococcus saprophyticus*
C. *Staphylococcus capitis*
D. *Staphylococcus aureus*
E. No listed answer is correct

Question #8
The laboratory reports an organism as Gram positive cocci in pairs that is alpha-hemolytic. Which of the following can this result be?
A. *Streptococcus pyogenes*
B. *Streptococcus agalactieae*
C. *Streptococcus pneumoniae*
D. Viridans group Streptococci
E. A and B are both correct
F. C and D are both correct

Question #9
The laboratory reports an organism as Gram positive cocci in pairs that is beta-hemolytic. Which of the following can this result be?
A. *Streptococcus agalactieae*
B. *Streptococcus pneumoniae*
C. *Streptococcus pyogenes*
D. Viridans group Streptococci
E. A and C are both correct
F. B and D are both correct

Question #10
The laboratory reports an organism as Gram positive cocci in pairs and chains and no additional information is available at this time. Which of the following is NOT the organism growing?
A. *Enterococcus faecalis*
B. *Streptococcus pyogenes*
C. *Streptococcus pneumoniae*
D. *Staphylococcus aureus*

Question #11
The laboratory reports an organism as Gram negative rod, non-fermenting. Which one of the following can this be?
A. *E. coli*
B. *Klebsiella pneumoniae*
C. *Pseudomonas aeruginosa*
D. *Proteus mirabilis*

Question #12
The laboratory identifies an organism as a Gram negative anaerobe. Which of the following can it be?
A. *Clostridium perfringens*
B. *Bacteroides fragilis*
C. *Peptostreptococcus* sp.
D. *Proprionobacterium acnes* (now called *Cutibacterium acnes*)

Question #13
Which of the following best describes *Staphylococcus aureus*?
A. Gram positive cocci, pairs, coagulase-negative, catalase negative
B. Gram positive cocci, clusters coagulase-negative, catalase positive
C. Gram positive cocci, clusters, coagulase-positive, catalase negative
D. Gram positive cocci, clusters, coagulase-positive, catalase positive

Question #14
True or false: Streptococci are catalase negative, while Staphylococci are catalase positive.

Question #15
The microbiology laboratory identifies an organism as being oxidase-negative. Which one of the following can it be?
A. *Pseudomonas* sp.
B. *Neisseria* sp.
C. *E. coli*
D. *Moraxella* sp.

Question #16
Which one of the following is NOT an atypical organism?
A. *Legionella*
B. *Mycoplasma*
C. *Chlamydia*
D. *Salmonella*

Question #17
The microbiology laboratory reports that a sputum sample has been found to be AFB-positive. Which of the following organisms is most likely to cause this positive result?
A. *Mycobacterium tuberculosis*
B. *Mycobacterium leprae*
C. *Mycobacterium abscessus*
D. *Mycobacterium mucogenicum*

Question #18
The microbiology lab reports an organism as "Gram variable", which one of the following is this likely to be?
A. *Staphylococcus aureus*
B. *Haemophilus influenzae*
C. *Acinetobacter baumannii*
D. *Neisseria meningitides*

Question #19
The microbiology lab reports an organism as a Gram negative "diplococci", which one of the following is this likely to be?
A. *Staphylococcus aureus*
B. *Haemophilus influenzae*
C. *Pseudomonas aeruginosa*
D. *Neisseria meningitidis*

Question #20
The microbiology lab reports an organism as "coccobacilli", which one of the following is this likely to be?
A. *Staphylococcus aureus*
B. *Haemophilus influenzae*
C. *coli*
D. *Neisseria meningitides*

Question #21
Which one of the following is NOT considered a "rapid growing" Mycobacterium species?
A. *Mycobacterium abscessus*
B. *Mycobacterium cheloniae*
C. *Mycobacterium tuberculosis*
D. *Mycobacterium fortuitum*

Question #22
Which of the following organisms is NOT a spirochete?
A. *Treponema pallidum* (causes syphilis)
B. *Trypanosoma cruzi* (causes Chagas disease)
C. *Borrellia burgdorferi* (causes Lyme disease)
D. *Treponema pallidum pertenue* (causes Yaws)

Question #23
Which one of the following is NOT an encapsulated bacterium?
A. *Haemophilus influenzae*
B. *Streptococcus pneumoniae*
C. *Staphylococcus aureus*
D. *Niesseria meningitidis*

Question #24
Which of the following is a urea splitting organism?
A. *Stenotrophomonas maltophilia*
B. *Proteus mirabilis*
C. *E. coli*
D. *Streptococcus pyogenes*

Question #25
Which organism could a microbiology lab report as "branching Gram positive rods."
A. *Nocardia* sp.
B. *Actinomycetes* sp.
C. A and B
D. None of the above

ANSWERS

Question #1 answer: B. The lowest drug concentration that will inhibit visual bacterial growth after overnight incubation

Question #2 answer: B. Discriminatory concentrations used to interpret whether a bacteria should be labeled as susceptible, intermediate, or resistant

Question #3 answer: A. Susceptible
NOTE: Even though an MIC of 2 mcg/mL for vancomycin to MRSA is considered "susceptible" vancomycin should likely be avoided, because "high MIC MRSA" to vancomycin has been associated with treatment failures. This is a specific exception relevant to clinical practice. It is unusual for clinicians to avoid a drug when the MIC value in the "susceptible" range.

Question #4 answer: B. First = Purple, Second = Pink

Question #5 answer: C. BMD (broth microdilution)
NOTE 1: Molecular rapid diagnostic tests are revolutionizing clinical microbiology because they are able to identify organisms and drug resistance hours or even days before conventional methods. This mean we can get patients on the right drugs faster if we use the data. NOTE 2: Broth microdilution is a method to test bacterial sensitivity to antimicrobials that requires 16-24 hours of incubation time.

Question #6 answer: C. *Staphylococcus aureus*

Question #7 answer: D. *Staphylococcus aureus*
NOTE: Staphylococci are Gram positive cocci in clusters or tetrads. *Staphylococcus aureus* is the only one that is coagulase positive. Other Staphylococci are coagulase negative, sometimes called "CoNS".

Question #8 answer: F. C and D are both correct

Question #9 answer: E. A and C are both correct

Question #10 answer: D. *Staphylococcus aureus*
NOTE: *S. aureus* is in clusters or tetrads while Streptococci and Enterococci are in chains or pairs. Enterococcus is gamma-hemolytic.

Question #11 answer: C. *Pseudomonas aeruginosa*
NOTE: "BAPAS" is sometimes used as an acronym to help remember some of the Gram negative rods B - Burkholderia A - Acinetobacter P - Pseudomonas A - Alcaligenes S - Stenotrophomonas

Question #12 answer: B. *Bacteroides fragilis*
NOTE: A, C, and D are Gram positive anaerobes.

Question #13 answer: D. Gram positive cocci, clusters, coagulase-positive, catalase positive

Question #14 answer: TRUE

Question #15 answer: C. *E. coli*
NOTE: Other listed answers are oxidase positive

Question #16 answer: D. *Salmonella*
NOTE 1: Atypical bacteria are those that do not color with Gram staining, but rather remain colorless. They are not Gram negative or Gram positive.; NOTE 2: Be careful not to confuse the terms Mycobacterium and Mycoplasma

Question #17 answer: A. *Mycobacterium tuberculosis*
NOTE 1: All mycobacterium are AFB-positive, but *Mycobacterium tuberculosis* is the most common to encounter in practice; NOTE 2: AFB = acid fast bacillus; NOTE 3: *Actinomyces sp., Nocardia sp.,* and *Rhotococcus equi* can also be AFB-positive

Question #18 answer: C. *Acinetobacter baumannii*
NOTE: Gram variable refers to upon performing a Gram stain, the organism appears both purple (for Gram positive) and pink (for Gram negative).

Question #19 answer: D. *Neisseria meningitidis*
NOTE: Diplococci are organisms that occur in pairs of cocci (circle shape). Moraxella catarrhalis and Acinetobacter spp. are also Gram negative diplococci. Staph. aureus is Gram positive clusters. Pseudomonas is gram negative bacilli (aka rods).

Question #20 answer: B. *Haemophilus influenzae*
NOTE: Coccobacilli are bacteria that occur in a shape intermediate between cocci (spherical) and bacilli (rod).

Question #21 answer: C. *Mycobacterium tuberculosis*
NOTE: A, B, and C are the main 3 rapid growing mycobacterium. Some of the lesser-known rapid growers are *Mycobacterium smegmatis, Mycobacterium mucogenicum*, and *Mycobacterium peregrinum.*

Question #22 answer: B. *Trypanosoma cruzi* (causes Chagas disease)
NOTE: Spirochetes are organisms that are twisted and appear to be in the shape of a corkscrew.

Question #23 answer: C. *Staphylococcus aureus*
NOTE: The spleen plays an important role in defending the body against encapsulated bacterium. Functional or anatomical asplenia is an indication for vaccination versus answers A, B, and D.

Question #24 answer: B. *Proteus mirabilis*
NOTE 1: Other urea splitting organisms include *Pseudomonas, Klebsiella, Staphylococcus*, and *Mycoplasma.*; NOTE 2: Struvite stones are potentiated by urea splitting bacteria, which hydrolyze urea into ammonium that results in higher urine pH.

Question #25 answer: C. A and B

Core Antimicrobial Spectra Rapid Fire Test

Question #1: What is the drug of choice for pan-sensitive Enterococci?

Question #2: What is the drug of choice for ampicillin-resistant Enterococci?

Question #3: What are 3 drugs that can be options for ampicillin-resistant and vancomycin-resistant Enterococci (VRE)?

Question #4: What is the drug of choice for *Corynebacterium jeikeium*?

Question #5: What is the drug of choice for *Stenotrophomonas maltophilia*?

Question #6: What is the drug of choice for *Listeria monocytogenes*?

Question #7: What is the drug of choice for Aspergillus?

Question #8: What is the drug of choice for *Candida albicans*?

Question #9: What is the drug class of choice for *Candida krusei*?

Question #10: Name at least 10 drugs with activity versus *Pseudomonas aeruginosa*.

Question #11: Name at least 10 drugs with activity versus methicillin-resistant *Staphylococcus aureus* (MRSA).

Question #12: What class of drugs is considered to be the drugs of choice versus most extended-spectrum beta-lactamase producing organisms (ESBL+)?

Question #13: Comparing ertapenem to meropenem, what coverage does ertapenem lack?

Question #14: What is the drug of choice for neurosyphilis?

Question #15: Name 3 drugs that can be used for *Clostridium difficile*.

Question #16: Name 3 drug classes that should come to mind when you need to treat infection due to an atypical organism.

Question #17: Name at least 3 oral drugs that are commonly considered when anaerobic coverage is desired.

Question #18: What oral drug is commonly used for cytomegalovirus (CMV)?

Question #19: What injectable drug is commonly used for cytomegalovirus (CMV)?

Question #20: What is the major organism that tigecycline does not have activity against?

Question #21: Name 2 drugs with only Gram negative activity.

Question #22: What Candida species can be either susceptible, intermediate / dose dependent-susceptible, or resistant to uconazole?

Question #23: Why are levofloxacin and moxifloxacin considered respiratory fluoroquinolones, while ciprofloxacin is not?

Question #24: What is the drug of choice for beta-hemolytic Streptococci (*e.g., Streptococcus pyogenes* and *Streptococcus agalactiae*)?

Question #25: What is the drug of choice for *Clostridium perfringens* (gas gangrene)?

Question #26: What is the drug of choice for infection due to Lyme Disease (*Borrelia burgdorferi*)?

ANSWERS

Question #1 Answer: Ampicillin

Question #2 Answer: Vancomycin

Question #3 Answer: 1. Linezolid (Zyvox) 2. Daptomycin (Cubicin, Cubicin RF) 3. Tigecycline (Tygacil)
NOTE: There are others, but these are the 3 most common therapies to consider.

Question #4 Answer: Vancomycin (Vancocin)

Question #5 Answer: Sulfamethoxazole-trimethoprim (Bactrim, Septra)

Question #6 Answer: Ampicillin

Question #7 Answer: Voriconazole (Vfend)

Question #8 Answer: Fluconazole (Diflucan)

Question #9 Answer: An echinocandin (micafungin [Mycamine], anidulafungin [Eraxis] or caspofungin [Cancidas])

Question #10 Answer: 1. Piperacillin-tazobactam (Zosyn) 2. Ceftazidime (Fortaz) 3. Cefepime (Maxipime) 4. Ceftazidime-avibactam (Avycaz) 5. Ceftolozane-tazobactam (Zerbaxa) 6. Cefiderocol (Fetroja) 7. Meropenem (Merrem) 8. Meropenem-vaborbactam (Vabomere [not really better than meropenem alone for Pseudomonas] 9. Imipenem-cilastatin (Primaxin) 10. Imipenem-cilastatin-relebactam (Recarbrio) 11. Aztreonam (Azactam, Cayston for inhaled) 12. Ciprofloxacin (Cipro) 13. Levofloxacin (Levaquin) 14. Delafloxacin (Baxdela) 15. Gentamicin 16. Tobramycin (TOBI for inhaled) 17. Amikacin (Arikayce for inhaled) 18. Polymyxin B 19. Colistin (polymyxin E) 20. Fosfomycin (Monurol) 21. Rifampin (Rifadin)

Question #11 Answer: 1. Sulfamethoxazole-trimethoprim (Bactrim, Septra) 2. Clindamycin (Cleocin) 3. Doxycycline (Doryx) 4. Tetracycline 5. Minocycline (Minocin) 6. Tigecycline (Tygacil) 7. Vancomycin (Vancocin) 8. Daptomycin (Cubicin, Cubicin RF) 9. Telavancin (Vabitv) 10. Oritavancin (Orbactiv, Kimyrsa) 11. Dalbavancin (Dalvance) 12. Linezolid (Zyvox) 13. Tedizolid (Sivextro) 14. Ceftaroline (Teflaro) 15. Quinupristin-dalfopristin (Synercid) 16. Fosfomycin (Monurol) 17. Rifampin (Rifadin) 18. Delafloxacin (Baxdela)
NOTE: Aminoglycosides can have activity, but need to be used as part of combination therapy so were not included here. Rifampin should only be used as a part of combination therapy for MRSA.

Question #12 Answer: Carbapenems (ertapenem [Invanz], meropenem [Merrem], imipenem-cilastatin [Primaxin], doripenem [Doribax])

Question #13 Answer: Acinetobacter, Pseudomonas, Enterococci
NOTE: You can use the acronym "APE" to remember this. Also, meropenem coverage for Enterococci is not perfect.

Question #14 Answer: Aqueous penicillin G

Question #15 Answer: 1. Metronidazole (Flagyl) 2. Oral vancomycin (Vancocin) 3. Fidaxomicin (Dificid)
NOTE: There are others, but these 3 are the main therapies to consider. Metronidazole is no longer preferred first-line.

Question #16: Answer: 1. Macrolides 2. Fluoroquinolones 3. Tetracyclines
NOTE: Some examples of atypical organisms include Mycoplasma, Chlamydia, and Legionella

Question #17 Answer: 1. Metronidazole (Flagyl) 2. Clindamycin (Cleocin) 3. Amoxicillin-clavulanic acid (Augmentin)

Question #18 Answer: Valganciclovir (Valcyte) – Be careful not to confuse with valacyclovir (Valtrex)

Question #19 Answer: Ganciclovir

Question #20 Answer: *Pseudomonas aeruginosa*

Question #21 Answer: 1. Aztreonam (Azactam, Cayston for inhaled) 2. Colistin (polymyxin E) 3. Polymyxin B

Question #22 Answer: *Candida glabrata*
NOTE: If you were thinking *Candida krusei*, that is not correct because this organism is always resistant to fluconazole. *Candida albicans* can be fluconazole resistant, but that is rare.

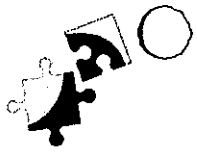
Question #23 Answer: Levofloxacin (Levaquin) and moxifloxacin (Avelox) have superior activity against the common respiratory pathogen *Streptococcus pneumoniae*.
NOTE: It is a common misconception that ciprofloxacin is not a respiratory fluoroquinolone because it does not penetrate the lungs well. This is not true. Ciprofloxacin does penetrate the lungs well. Levofloxacin and moxifloxacin also penetrate the lungs well.

Question #24 Answer: Penicillin

Question #25 Answer: Penicillin

Question #26 Answer: Doxycycline (Doryx)

Mechanisms Of Actions Match Game I



ANSWER BANK

amikacin, amphotericin B, avibactam, azithromycin, aztreonam, caspofungin, cefiderocol, ciprofloxacin, daptomycin, fluconazole, flucytosine, linezolid, nitrofurantoin, rifampin, sulfamethoxazole-trimethoprim, vancomycin

1. Interferes with ergosterol synthesis, which is the principal sterol in the fungal cell membrane.
2. Inhibits 1,3-beta-D-glucan synthesis, a component of the fungal cell wall.
3. Binds to ergosterol and alters cell membrane permeability in susceptible fungi, causing leakage of cell components and subsequent fungal cell death.
4. Penetrates the cells of fungi, where it is converted to fluorouracil, which then competes with uracil, thus interfering with fungal RNA and protein synthesis.
5. Works on susceptible bacteria by inhibiting RNA-dependent protein synthesis at the chain elongation step. It binds to the 50S ribosomal subunit, which blocks transpeptidation.
6. Inactivates some beta-lactamases, which can protect beta-lactam antibiotics from being hydrolyzed.
7. Works by causing depolarization of the cell membrane in sensitive bacteria.
8. Interferes with bacterial DNA synthesis in susceptible bacteria by inhibiting DNA gyrase (topoisomerase II) & topoisomerase IV.
9. Inhibits bacterial RNA synthesis by binding the beta subunit of DNA-dependent RNA polymerase, blocking RNA transcription.
10. Inhibits bacterial cell wall synthesis through binding to penicillin binding protein 3. Chelates ferric ions and uses bacterial iron transport systems, which has been called a "Trojan Horse" strategy and translates to higher concentrations in the periplasmic space of susceptible Gram negative bacteria.
11. Binds to penicillin binding proteins (PBP), interfering with bacterial cell wall synthesis. Has a high affinity for PBP-3.
12. Inhibits cell wall synthesis in susceptible bacteria by blocking glycopeptide polymerization via binding tightly to the D-alanyl-D-alanine portion of the cell wall precursor.
13. Works on susceptible bacteria through interfering with bacterial protein synthesis. Binds to the bacterial 23S ribosomal RNA of the 50S subunit, which prevents formation of a functional 70S initiation complex essential to bacterial translation.
14. Is reduced by bacterial flavoproteins to reactive intermediates that inactivate or alter bacterial ribosomal proteins. This leads to inhibition of protein synthesis, aerobic energy metabolism, DNA, RNA and cell wall synthesis.
15. Interferes with bacterial folic acid synthesis and growth by blocking dihydrofolic acid formation from para-aminobenzoic acid.
16. Inhibits bacterial RNA synthesis by binding to the beta subunit of DNA-dependent RNA polymerase, which blocks RNA transcription.

ANSWERS

1. Interferes with ergosterol synthesis, which is the principal sterol in the fungal cell membrane. **Fluconazole (Diflucan)**

2. Inhibits 1,3-beta-D-glucan synthesis, a component of the fungal cell wall. **Caspofungin (Cancidas)**

3. Binds to ergosterol and alters cell membrane permeability in susceptible fungi, causing leakage of cell components and subsequent fungal cell death. **Amphotericin B (Abelcet, Ambisome)**

4. Penetrates the cells of fungi, where it is converted to fluorouracil, which then competes with uracil, thus interfering with fungal RNA and protein synthesis. **Flucytosine (Ancobon)**

5. Works on susceptible bacteria by inhibiting RNA-dependent protein synthesis at the chain elongation step. It binds to the 50S ribosomal subunit, which blocks transpeptidation. **Azithromycin (Zmax)**

6. Inactivates some beta-lactamases, which can protect beta-lactam antibiotics from being hydrolyzed. **Avibactam (available as ceftazidime-avibactam, Avycaz)**

7. Works by causing depolarization of the cell membrane in sensitive bacteria. **Daptomycin (Cubicin, Cubicin RF)**

8. Interferes with bacterial DNA synthesis in susceptible bacteria by inhibiting DNA gyrase (topoisomerase II) & topoisomerase IV. **Ciprofloxacin (Cipro)**

9. Inhibits bacterial RNA synthesis by binding the beta subunit of DNA-dependent RNA polymerase, blocking RNA transcription. **Amikacin (Arikayce)**

10. Inhibits bacterial cell wall synthesis through binding to penicillin binding protein 3. Chelates ferric ions and uses bacterial iron transport systems, which has been called a "Trojan Horse" strategy and translates to higher concentrations in the periplasmic space of susceptible Gram negative bacteria. **Cefiderocol (Fetroja)**

11. Binds to penicillin binding proteins (PBP), interfering with bacterial cell wall synthesis. Has a high affinity for PBP-3. **Aztreonam (Azactam, Cayston for inhaled)**

12. Inhibits cell wall synthesis in susceptible bacteria by blocking glycopeptide polymerization via binding tightly to the D-alanyl-D-alanine portion of the cell wall precursor. **Vancomycin (Vancocin)**

13. Works on susceptible bacteria through interfering with bacterial protein synthesis. Binds to the bacterial 23S ribosomal RNA of the 50S subunit, which prevents formation of a functional 70S initiation complex essential to bacterial translation. **Linezolid (Zyvox)**

14. Is reduced by bacterial flavoproteins to reactive intermediates that inactivate or alter bacterial ribosomal proteins. This leads to inhibition of protein synthesis, aerobic energy metabolism, DNA, RNA and cell wall synthesis. **Nitrofurantoin (Macrobid, Macrodantin)**

15. Interferes with bacterial folic acid synthesis and growth by blocking dihydrofolic acid formation from para-aminobenzoic acid. **Sulfamethoxazole-trimethoprim (Bactrim, Septra)**

16. Inhibits bacterial RNA synthesis by binding to the beta subunit of DNA-dependent RNA polymerase, which blocks RNA transcription. **Rifampin (Rifadin)**

Mechanisms Of Actions Match Game II

ANSWERS BANK

Baloxavir, bezlotoxumab, clindamycin, elbasvir, eravacycline, fosfomycin, grazoprevir, lefamulin, letermovir, metronidazole, methenamine, oseltamivir, polymyxin B, remdesivir, telavancin, valacyclovir, valganciclovir

1. Is an NS3/4A inhibitor, which blocks HCV NS3/A4 and interferes with proteolytic cleavage of HCV-encoded polyprotein essential for viral replication.
2. A prodrug, it works by inhibiting DNA synthesis and viral replication by competing with deoxyguanosine triphosphate for viral DNA polymerase.
3. A polymerase acidic endonuclease inhibitor active against influenza virus.
4. Blocks influenza neuraminidase, an enzyme involved in viral replication.
5. Acts as an analog of ATP and competes with natural ATP substrate for incorporation into RNA chains by the SARS-CoV-2 RNA-dependent polymerase, which results in delayed chain termination during viral RNA replication.
6. Inhibits the CMV DNA terminase complex (pUL51, pUL56, and pUL89) required for viral DNA processing and packaging.
7. Inhibits HCV NS5A which interferes with viral replication and virion assembly.
8. IA prodrug, it is phosphorylated to a substrate which competitively inhibits binding of deoxyguanosine triphosphate to DNA polymerase, resulting in inhibition of viral DNA synthesis.
9. Inhibits bacterial protein synthesis by binding to the peptidyl transferase center of the 50S bacterial ribosome, which in turn prevents the binding of transfer RNA for peptide transfer.
10. Interacts with DNA to interfere with the helical DNA structure/strands, which results in inhibition of protein synthesis and cell death for susceptible organisms.
11. Is hydrolyzed to formaldehyde and ammonia in acidic urine, which produces antibacterial effects.
12. Inactivates pyruvyl transferase (an enzyme critical for cell wall synthesis), which interferes with bacterial cell wall formation.
13. Inhibits the 30S ribosomal subunit of susceptible bacteria, which interferes with bacterial protein synthesis.
14. Inhibits protein synthesis in susceptible bacteria by binding to the 50S ribosomal subunit.
15. Works as a cationic detergent, damaging bacterial cytoplasmic membrane and causing leakage of intracellular contents.
16. Has both the mechanism of action for vancomycin (binding d-ala, d-ala) as well as the mechanism of action for daptomycin (causes depolarization).
17. Inhibits the RNA polymerase sigma subunit in susceptible organisms, which results in the inhibition of protein synthesis and cell death.
18. A human IgG1 monoclonal antibody that works by binding to and neutralizing *Clostridioides difficile* toxin B, which prevents toxic effects.

ANSWERS

1. Is an NS3/4A inhibitor, which blocks HCV NS3/A4 and interferes with proteolytic cleavage of HCV-encoded polyprotein essential for viral replication. **Grazoprevir (available as elbasvir/ grazoprevir, Zepatier)**

2. A prodrug of acyclovir, works by inhibiting DNA synthesis and viral replication by competing with deoxyguanosine triphosphate for viral DNA polymerase. **Valacyclovir (Valtrex)**

3. A polymerase acidic endonuclease inhibitor active against influenza virus. **Baloxavir marboxil (Xofluza)**

4. Blocks influenza neuraminidase, an enzyme involved in viral replication. **Oseltamivir (Tamiflu)**

5. Acts as an analog of ATP and competes with natural ATP substrate for incorporation into RNA chains by the SARS-CoV-2 RNA-dependent polymerase, which results in delayed chain termination during viral RNA replication. **Remdesivir (Veklury)**

6. Inhibits the CMV DNA terminase complex (pUL51, pUL56, and pUL89) required for viral DNA processing and packaging. **Letermovir (Prevymis)**

7. Inhibits HCV NS5A which interferes with viral replication and virion assembly. **Elbasvir (available as elbasvir/ grazoprevir, Zepatier)**

8. A prodrug of ganciclovir, is phosphorylated to a substrate which competitively inhibits binding of deoxyguanosine triphosphate to DNA polymerase, resulting in inhibition of viral DNA synthesis. **Valganciclovir (Valcyte)**

9. Inhibits bacterial protein synthesis by binding to the peptidyl transferase center of the 50S bacterial ribosome, which in turn prevents the binding of transfer RNA for peptide transfer. **Lefamulin (Xenleta)**

10. Interacts with DNA to interfere with the helical DNA structure/strands, which results in inhibition of protein synthesis and cell death for susceptible organisms. **Metronidazole (Flagyl)**

11. Is hydrolyzed to formaldehyde and ammonia in acidic urine, which produces antibacterial effects. **Methenamine (Hiprex, Urex)**

12. Inactivates pyruvyl transferase (an enzyme critical for cell wall synthesis), which interferes with bacterial cell wall formation. **Fosfomycin (Monurol)**

13. Inhibits the 30S ribosomal subunit of susceptible bacteria, which interferes with bacterial protein synthesis. **Eravacycline (Xerava)**

14. Inhibits protein synthesis in susceptible bacteria by binding to the 50S ribosomal subunit. **Clindamycin (Cleocin)**

15. Works as a cationic detergent, damaging bacterial cytoplasmic membrane and causing leakage of intracellular contents. **Polymyxin B**

16. Has both the mechanism of action for vancomycin (binding d-ala, d-ala) as well as the mechanism of action for daptomycin (causes depolarization). **Telavancin (Vibativ)**

17. Inhibits the RNA polymerase sigma subunit in susceptible organisms, which results in the inhibition of protein synthesis and cell death. **Fidaxomicin (Dificid)**

18. A human IgG1 monoclonal antibody that works by binding to and neutralizing *Clostridioides difficile* toxin B, which prevents toxic effects. **Bezlotoxumab (Zinplava)**

Mechanisms of Action Rapid Fire Test

Question #1
How do beta-lactams work? (e.g., penicillins, cephalosporins, and carbapenems)

Question #2
Are beta-lactams time-dependent killers or concentration dependent killers?

Question #3
How do fluoroquinolones work? (e.g., ciprofloxacin, moxifloxacin, levofloxacin, delafloxacin)

Question #4
How do aminoglycosides work?

Question #5
Are aminoglycosides time-dependent killers or concentration dependent killers?

Question #6
How does fidaxomicin work?

Question #7
How do macrolides other than fidaxomicin work? (e.g., erythromycin, clarithromycin, and azithromycin)

Question #8
How do tetracycline, doxycycline, minocycline, and tigecycline work?

Question #9
How do oxazolidinones work? (e.g., linezolid, tedizolid)

Question #10
How does clindamycin (a lincosamide) work?

Question #11
How does metronidazole work?

Question #12
How does vancomycin work?

Question #13
How does daptomycin work?

Question #14
How does telavancin work?

Question #15
How does oritavancin work?

Question #16
How does dalbavancin work?

Question #17
How does sulfamethoxazole-trimethoprim (Bactrim, Septra) work?

Question #18
How does rifampin work?

Question #19
How does nitazoxanide work?

Question #20
How do echinocandins work? (e.g., micafungin, anidulafungin, caspofungin)

Question #21
How do azole antifungals work? (e.g., fluconazole, itraconazole, posaconazole, voriconazole, isavuconazole)

Question #22
How do polyene antifungals work? (i.e., amphotericin B)

Question #23
How does the antifungal drug flucytosine work?

Question #24
How does the antiviral drug acyclovir work?

Question #25
How does the antiviral drug valacyclovir work?

Question #26
How does the antiviral drug ganciclovir work?

Question #27
How does the antiviral drug valganciclovir work?

Question #28
How does antiviral drug letermovir work?

Question #29
How does foscarnet work?

Question #30
How does cidofovir work?

Question #31
How do neuraminidase inhibitors work? (e.g. oseltamivir, zanamivir, peramivir)

ANSWERS

Question #1 answer: Bind to various to penicillin binding proteins (PBPs), which leads to interference with peptidoglycan cross-linkage and inhibition of cell wall biosynthesis.

Question #2 answer: They are **time-dependent** killers, which means the LONGER the concentration of drug at the site of infection is sufficient, the MORE bacterial killing will be achieved.

Question #3 answer: They bind to topoisomerase IV and/or DNA gyrase (aka topoisomerase II). The DNA gyrase activity inhibits relaxation of supercoiled DNA, which causes DNA strand breakage. The topoisomerase IV activity interrupts separation of interlinked daughter chromosomes after DNA replication.

Question #4 answer: They interfere with bacterial protein synthesis through binding with the 30S ribosomal subunit, which results in a dysfunctional bacterial cell membrane.

Question #5 answer: They are **concentration-dependent** killers, which means the HIGHER the concentration of drug at the site of infection, the MORE bacterial killing will be achieved.

Question #6 answer: It interferes with protein synthesis by inhibiting the RNA polymerase sigma subunit.

Question #7 answer: They inhibit bacterial protein synthesis through binding with the 50S ribosomal subunit.

Question #8 answer: They inhibit bacterial protein synthesis through binding with the 30S ribosomal subunit.

Question #9 answer: They interfere with protein synthesis by binding to the 23S RNA of the 50S ribosomal subunit, which inhibits formation of a functional 70S initiation complex.

Question #10 answer: It inhibits bacterial protein synthesis through binding with the 50S ribosomal subunit.

Question #11 answer: It interacts with DNA to interfere with the helical DNA structure/strands, which results in inhibition of protein synthesis and cell death for susceptible organisms.

Question #12 answer: Inhibits cell wall synthesis in susceptible bacteria by blocking glycopeptide polymerization via binding tightly to the D-alanyl-D-alanine portion of the cell wall precursor
NOTE: Vancomycin exhibits AUC:MIC killing versus MRSA and a typical goal is to have an AUC:MIC > 400.

Question #13 answer: It causes permeabilization and depolarization of the bacterial cell membrane

Question #14 answer: Inhibits cell wall synthesis in susceptible bacteria by blocking glycopeptide polymerization via binding tightly to the D-alanyl-D-alanine portion of the cell wall precursor AND alters cell permeability.

Question #15 answer: It blocks the transglycosylation step of peptidoglycan synthesis, inhibiting transpeptidation (cross-linking), and perturbations of membrane potential (depolarization and increased permeability).

Question #16 answer: It interferes with cell wall synthesis by binding to the D-alanyl-D-alanine terminus of the stem pentapeptide in nascent cell wall peptidoglycan, thus preventing cross-linking.

Question #17 answer: Sulfamethoxazole interferes with bacterial folic acid synthesis by disrupting dihydrofolic acid formation from para-aminobenzoic acid.
Trimethoprim interferes with sequential inhibition of enzymes in the folic acid pathway by inhibiting dihydrofolic acid reduction to tetrahydrofolate.

Question #18 answer: It inhibits DNA-dependent RNA polymerase activity.

Question #19 answer: It interferes with the pyruvate:ferredoxin oxidoreductase (PFOR) enzyme-dependent electron transfer reaction which is essential to anaerobic energy metabolism.

Question #20 answer: They inhibit the synthesis of 1,3-β-D- glucan, an essential component of fungal cell walls, which is not present in mammalian cells.

Question #21 answer: They interfere with ergosterol synthesis through inhibition of fungal cytochrome P450 dependent enzyme lanosterol 14-alpha-demethylase.

Question #22 answer: They bind to ergosterol and alter permeability of the cell membrane. Occurs differently than the azoles.

Question #23 answer: It converts to fluorouracil after entering the cell, then subsequently converts into several metabolites. The metabolites inhibit protein synthesis by being falsely incorporated into fungal RNA or interfere with the biosynthesis of fungal DNA through the inhibition of the enzyme thymidylate synthetase.

Question #24 answer: Thymidine kinase converts acyclovir into acyclovir monophosphate, which is then further converted into diphosphate by cellular guanylate kinase, then into triphosphate by a number of cellular enzymes.
Acyclovir triphosphate stops replication of herpes viral DNA through: (1) competitive inhibition of viral DNA polymerase, (2) incorporation into and termination of the growing viral DNA chain, and (3) inactivation of the viral DNA polymerase.

Question #25 answer: Valacyclovir is a pro-drug that is converted into acyclovir in vivo.
Thymidine kinase converts acyclovir into acyclovir monophosphate, which is then further converted into diphosphate by cellular guanylate kinase, then into triphosphate by a number of cellular enzymes.
Acyclovir triphosphate stops replication of herpes viral DNA through: (1) competitive inhibition of viral DNA polymerase, (2) incorporation into and termination of the growing viral DNA chain, and (3) inactivation of the viral DNA polymerase.

Question #26 answer: In CMV-infected cells, ganciclovir is initially phosphorylated to ganciclovir monophosphate by the viral protein kinase, pUL97. Further phosphorylation occurs by cellular kinases to produce ganciclovir triphosphate, which is then slowly metabolized intracellularly. As the phosphorylation is largely dependent on the viral kinase, phosphorylation of ganciclovir occurs preferentially in virus-infected cells. The virustatic activity of ganciclovir is due to inhibition of the viral DNA polymerase, pUL54, by ganciclovir triphosphate.

Question #27 answer: Valganciclovir is a pro-drug that is converted into ganciclovir in vivo.
In CMV-infected cells, ganciclovir is initially phosphorylated to ganciclovir monophosphate by the viral protein kinase, pUL97. Further phosphorylation occurs by cellular kinases to produce ganciclovir triphosphate, which is then slowly metabolized intracellularly. As the phosphorylation is largely dependent on the viral kinase, phosphorylation of ganciclovir occurs preferentially in virus-infected cells. The virustatic activity of ganciclovir is due to inhibition of the viral DNA polymerase, pUL54, by ganciclovir triphosphate.

Question #28 answer: It inhibits the CMV DNA terminase complex (pUL51, pUL56, and pUL89) which is required for viral DNA processing and packaging. It affects the production of proper unit length genomes and interferes with virion maturation.

Question #29 answer: It exerts its antiviral activity by a selective inhibition at the pyrophosphate binding site on virus-specific DNA polymerases.

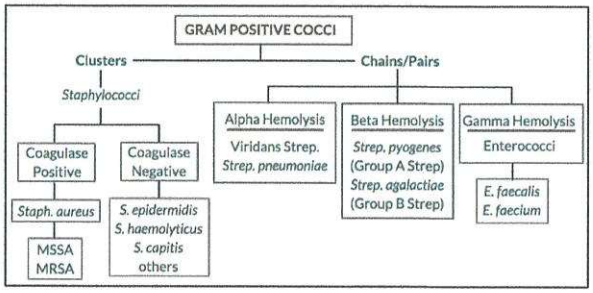
Question #30 answer: It suppresses cytomegalovirus (CMV) replication by selective inhibition of viral DNA synthesis.

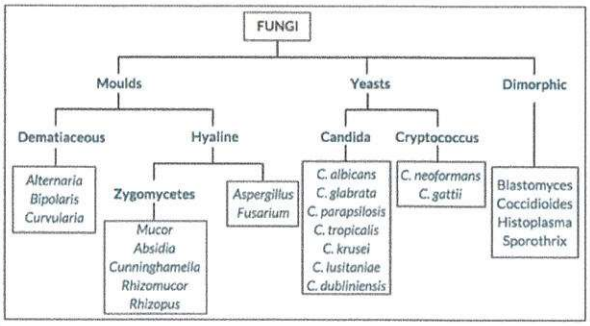
Question #31 answer: They inhibit influenza virus neuraminidase, which effects the release of viral particles.

Bugs & Drugs Cheat Sheet

When You See...	Consider Using...
GRAM POSITIVES	
MSSA	**Oral**: cephalexin, cefadroxil, dicloxacillin, amox/clav **IV**: cefazolin, oxacillin, nafcillin
MRSA	**Oral**: SMX/TMP, doxycycline, clindamycin, linezolid, tedizolid, omadacycline, delafloxacin; **IV**: vancomycin, daptomycin, telavancin, dalbavancin, oritavancin, ceftaroline, tigecycline, eravacycline -All oral options have IV formulations
Enterococci	Ampicillin, then vancomycin; if VRE: linezolid, daptomycin, oritavancin, tigecycline, omadacycline, eravacycline -For cystitis only: nitrofurantoin, fosfomycin
Strep. pyogenes or *Strep. agalactiae*	Penicillin, amoxicillin, clindamycin
Strep. pneumoniae or Viridans group Streptococci	Ceftriaxone, levofloxacin, amoxicillin, amoxicillin-clavulanic acid (⚠ beware penicillin & macrolide resistance)
Listeria monocytogenes	Ampicillin
GRAM NEGATIVES	
Pseudomonas aeruginosa	**Oral**: ciprofloxacin, levofloxacin, delafloxacin **IV**: piperacillin-tazobactam, ceftazidime, ceftazidime-avibactam, cefepime, ceftolozane-tazobactam, cefiderocol, imipenem-cilastatin +/- relebactam, meropenem, aztreonam, aminoglycosides, polymyxins
E. coli, Klebsiella	**Oral**: cephalexin, amoxicillin-clavulanic acid, SMX/TMP, ciprofloxacin, levofloxacin, delafloxacin -For cystitis only: nitrofurantoin, fosfomycin **IV**: ceftriaxone, ampicillin-sulbactam (⚠ resistance), cefepime, piperacillin-tazobactam, carbapenems
ESBL-producer / Drug-Resistant GNR	Carbapenems, ceftolozane-tazobactam, ceftazidime-avibactam, meropenem-vaborbactam, imipenem-cilastatin-relebactam, cefiderocol, polymyxins, aminoglycosides, tigecycline, omadacycline, eravacycline -For cystitis only: nitrofurantoin, fosfomycin
Carbapenem resistant GNR	ESBL-producer drug list minus carbapenem alone
NDM producer	Aztreonam + (MERO/VAB or CAZ/AVI), cefiderocol
Stenotrophomonas	SMX/TMP, levofloxacin, minocycline
Salmonella typhi	Fluoroquinolone, SMX/TMP, ceftriaxone
FUNGI	
Candida albicans	Fluconazole
Candida glabrata	Echinocandin, but can use fluconazole if susceptible
Candida krusei	Micafungin, anidulafungin, or caspofungin
Candida auris	Micafungin, anidulafungin, or caspofungin
Aspergillus	Voriconazole
MISCELLANEOUS PATHOGENS	
Anaerobes	**Oral:** metronidazole, clindamycin, amoxicillin-clavulanic acid, moxifloxacin **IV**: ampicillin-sulbactam, piperacillin-tazobactam, cefoxitin, cefotetan, ertapenem, tigecycline
Clostridioides difficile (formerly *Clostridium difficile*)	Oral vancomycin or fidaxomicin → Metronidazole no longer preferred
Atypical organisms	Macrolides, fluoroquinolones, tetracyclines, lefamulin
Cryptosporidium parvum	Nitazoxanide
Cystoisospora sp., *Isospora*	SMX/TMP
Borrelia burgdorferi, Lyme	Doxycycline
Treponema pallidum, Syphilis	Penicillin
Mycobacterium tuberculosis	Rifampin + isoniazid + pyrazinamide + pyridoxine + ethambutol – "RIPPE"
Mycobacterium avium (MAC)	Clarithromycin+ethambutol (treatment), azithromycin (prophylaxis)
Pneumocystis Pneumonia	SMX/TMP (treatment] or prophylaxis)
Toxoplasma gondii	Pyrimethamine+sulfadiazine +leucovorin (treatment); SMX/TMP (prophylaxis)

See This...	Consider This...
Bacterial vaginosis	Metronidazole
Chlamydia	Doxycycline, azithromycin
Gonorrhea	Ceftriaxone
Cystitis	Nitrofurantoin
ESBL E. coli cystitis	Fosfomycin
Prostatitis	Fluoroquinolones, SMX/TMP
MSSA bacteremia	Oxacillin, nafcillin, cefazolin
MRSA pneumonia	Linezolid or vancomycin
Enterococcal endocarditis	Ceftriaxone + ampicillin
Viridans Strep endocarditis	Aqueous penicillin G
Yeast in blood/ Candidemia	Echinocandin
Malaria needing IV treatment	Artesunate
Cryptococcal meningitis	Amphotericin B + flucytosine
Strongyloidiasis	Ivermectin
Chickenpox or shingles	Valacyclovir, acyclovir
Hepatitis B	Tenofovir, entecavir
Aztreonam	Gram negatives only
Polymyxin or colistin	Gram negatives only
Glycopeptides	Gram positives only
Cephalosporins	Not for anaerobes
Ertapenem	Not for APE: Acinetobacter, Pseudomonas, Enterococci
Clindamycin	Not for B frag
Vancomycin PO or fidaxomicin	C difficile only
Tigecycline, omadacycline, or eravacycline	Not for PPP: Providencia, Pseudomonas, or Proteus
Rifampin	Not for monotherapy
Fluconazole	Not for Candida krusei





ABBREVIATIONS: Amox/clav = amoxicillin/clavulanic acid, CAZ/AVI = ceftazidime/avibactam, ESBL = extended-spectrum beta-lactamase, GNR = Gram negative rod, IV = intravenous, MERO/VAB = meropenem/vaborbactam, MRSA = methicillin-resistant *S.* aureus, MSSA =methicillin-susceptible *S.* aureus, NDM = New Delhi metallo-beta-lactamase, PIP/TAZ = piperacillin/tazobactam, SMX/TMP = sulfamethoxazole/trimethoprim, VRE = vancomycin resistant Enterococci

Antibiotics Key Points Cheat Sheet

GLOBAL KEY POINT: Use antibiotics only when indicated. Right diagnosis. Right time. Right drug. Right Route. Right dose. Right duration.

CLASS	DRUG EXAMPLE	KEY SIDE EFFECTS	KEY POINTS
β-lactams	Ampicillin, Cephalexin, Meropenem	Diarrhea, seizures (at high doses), allergy (beware false allergy), with oxacillin/nafcillin beware AST/ALT elevation	• Frequently first-line antibiotics due to safety and efficacy profiles • Only ~10% of penicillin allergy labels represent a true penicillin allergy
Fluoroquinolones	Ciprofloxacin Levofloxacin Moxifloxacin Delafloxacin	FDA Boxed Warnings: Tendonitis, tendon rupture, CNS effects, peripheral neuropathy, can worsen existing myasthenia gravis Other: hypoglycemia (including coma), altered mental health, aortic dissection, QTc prolongation, photosensitivity, suicidal thoughts, diarrhea (including *C. diff* infection)	• Levo, cipro, and dela can be oral options for *Pseudomonas aeruginosa* • Avoid moxifloxacin for UTI (achieves low urine concentrations) • Only use FQs when indicated, avoid when possible • Cipro is a go-to for prostatitis, but beware *E. coli* resistance to FQs • Beware oral FQs bind to cations like calcium and aluminum
Aminoglycosides	Tobramycin, Amikacin	Ototoxicity, nephrotoxicity	• Only use monotherapy for UTI
Oxazolidinones	Linezolid, Tedizolid	Thrombocytopenia, peripheral neuropathy, optic neuritis	• Beware DDIs w/ SSRIs and MAOIs that may lead to Serotonin Syndrome • Generally avoid for MRSA bacteremia, but a good option for MRSA pneumonia
Tetracyclines	Doxycycline	Esophagitis (with oral route), photosensitivity Avoid in 8 years or less d/t tooth discoloration, enamel hypoplasia, and bone growth inhibition (this is a debated topic)	• Have a wide range of uses including for malaria, mycobacterium, atypicals, MRSA skin infection, acne, syphilis, Lyme disease, and more! • Doxy does not require dose adjustments for renal function
Macrolides	Azithromycin	QTc prolongation, diarrhea (erythromycin is a motilin agonist)	• Can be used for atypical organisms • DDIs more common w/ clarithromycin
Rifamycins	Rifampin	Hepatotoxicity, discoloration of secretions (red/orange)	• Potent inducer of CYP enzymes (will reduce levels of other drugs) • Rarely indicated as monotherapy • Penetrates biofilms on hardware (plates, screws, prosthetic valves)

Note: Side effect risks vary between drugs in a given class. For more information, most are detailed in the package insert of each drug.

DRUG	CLASS	KEY SIDE EFFECTS	KEY POINTS
Vancomycin IV	Glycopeptide	Nephrotoxicity, infusion-related histamine release (infuse each gram over at least 60 minutes)	• Over-used and can often be discontinued • MRSA nasal swabs have a high negative predictive value for pneumonia • Requires individualized dosing/monitoring to ensure safety/efficacy
Daptomycin	Lipopeptide	CPK elevation, rhabdomyolysis, eosinophilic pneumonia	• Do not use for pneumonia, inactivated by surfactant • Adjust dose from every 24 hours to every 48 hours when CrCl < 30
Metronidazole	Nitroimidazole	FDA Boxed Warning: carcinogenic in mice and rats Other: Metallic taste, nausea, peripheral neuropathy, CNS effects	• Avoid concomitant alcohol intake due to risk of disulfiram like reaction (debated) • Has fallen out of favor as a therapy for *C. difficile* infection
Clindamycin	Lincosamide	Diarrhea, including *C. difficile* infection	• Common go-to for penicillin allergic patients • Can be used for toxin mediation with Strep and Staph infections
SMX/TMP	Sulfa	Hyperkalemia, hypocalcemia, hyponatremia, blood dyscrasias (myelosuppression), dermatologic reactions/ allergy	• Hyperkalemia particularly problematic with high-dose IV, go oral ASAP • IV formulation has a high fluid load of D5W and short stability once mixed
Tigecycline	Glycylcycline	Nausea & vomiting!!!, AST/ALT elevation	• Not a good drug for bloodstream infections b/c does not stay in the serum
Nitrofurantoin	Nitrofuran	Pulmonary fibrosis w/ repeated or prolonged use	• Avoid if CrCl below 30 (note used to be 60, refer to Beers Criteria) • Do not use for upper UTI (pyelonephritis) or prostatitis
Fosfomycin	Phosphonic acid derivative	Generally well tolerated	• Do not use for upper UTI (pyelonephritis), limited role for prostatitis

Abbreviations: ASAP = as soon as possible, CNS = central nervous system, CYP = cytochrome P450, DDI = drug-drug interaction, FQ = fluoroquinolone, IV = intravenous, MAOI = monoamine oxidase inhibitor, SMX/TMP = sulfamethoxazole/trimethoprim, SSRI = selective serotonin reuptake inhibitor, UTI = urinary tract infection

Drugs of Choice Memorization Sheet

Drugs of Choice (generalization)

The drug of choice for syphilis (caused by _____, which is a _____) is _____.

The drug of choice for Lyme disease (caused by _____, which is a _____) is _____.

The drug of choice for *Enterococcus* spp (which are Gram _____ _____ that grow in _____ or _____ and are _____-hemolytic) is _____.

_____-resistant Enterococci can be treated with _____.

_____-resistant Enterococci are called _____.

Drugs that can potentially cover _____ include _____, _____, _____, _____, _____, _____, and _____.

The drug of choice for *Listeria monocytogenes* (which is a Gram _____ _____) is _____.

The drug of choice for *Streptococcus pyogenes* (aka _____, which grows as Gram _____ _____ in _____ or _____ and is _____-hemolytic) is _____. Sometimes _____ is added for toxin mediation.

The drug of choice for *Clostridium perfringens* (aka _____, which is an _____ Gram _____ ____) is _____.

There is no true drug of choice for *Clostridioides difficile* (an _____ Gram _____ ____), however _____ is a common first choice.

There is no true drug of choice for MSSA (which is a coagulase-_____ Gram _____ _____ that grows in _____ and lacks the _____ gene), however _____ (e.g., _____, _____) and _____ (e.g., _____, _____) are common go-to options.

There is no true drug of choice for MRSA (which is a _____-positive Gram _____ _____ that grows in _____ and has the _____ gene) however _____ is a common initial drug for empiric therapy in hospitalized patients.

_____, _____, and _____ provide important oral options for community-acquired MRSA infections.

The drug of choice for *Stenotrophomonas maltophilia* (which is a _____ Gram _____ _____) is _____.

A second-line drug for *Stenotrophomonas maltophilia* is _____.

The drug of choice for *Nocardia* spp (which is a weakly staining Gram _____ _____) is _____.

The drug of choice for *Aspergillus* spp (a type of _____) is _____.

_____ is generally considered the go-to drug for infections caused by *Candida* spp (which are yeasts). Beware _____-resistant *Candida* _____, *Candida* _____, or *Candida* _____.

ANSWERS

Drugs of Choice (generalization)

The drug of choice for syphilis (caused by _*Treponema pallidum*_, which is a _*spirochete*_) is _*penicillin*_.

The drug of choice for Lyme disease (caused by _*Borrelia burgdorferi*_, which is a _*spirochete*_) is _*doxycycline*_.

The drug of choice for *Enterococcus* spp (which are Gram _*positive*_ _*cocci*_ that grow in _*pairs*_ or _*chains*_ and are _*gamma*_-hemolytic) is _*ampicillin*_.

*Ampicillin*-resistant Enterococci can be treated with _*vancomycin*_.

*Vancomycin*-resistant Enterococci are called _*VRE*_.

Drugs that can potentially cover _*VRE*_ include _*daptomycin*_, _*oritavancin*_, _*linezolid*_, _*tedizolid*_, _*tigecycline*_, _*eravacycline*_, and _*omadacycline*_.

The drug of choice for *Listeria monocytogenes* (which is a Gram _*positive*_ _*bacilli*_) is _*ampicillin*_.

The drug of choice for *Streptococcus pyogenes* (aka _*Group A Strep*_, which grows as Gram _*positive*_ _*cocci*_ in _*pairs*_ or _*chains*_ and is _*beta*_-hemolytic) is _*penicillin*_. Sometimes _*clindamycin*_ is added for toxin mediation.

The drug of choice for *Clostridium perfringens* (aka _*gas gangrene*_, which is an _*anaerobic*_ Gram _*positive*_ _*rod*_) is _*penicillin*_.

There is no true drug of choice for *Clostridioides difficile* (an _*anaerobic*_ _*spore*_-forming Gram _*positive*_ _*rod*_), however _vanco PO_ is a common first choice.

There is no true drug of choice for MSSA (which is a coagulase-_*positive*_ Gram _*positive*_ _*cocci*_ that grows in _*clusters*_ and lacks the _*MecA*_ gene), however _*first gen cephs*_ (e.g., _*cefazolin*_, _*cephalexin*_) and _*anti-staphylococcal penicillins*_ (e.g., _*oxacillin*_, _*nafcillin*_) are common go-to options.

There is no true drug of choice for MRSA (which is a _*coagulase*_-positive Gram _*positive*_ _*cocci*_ that grows in _*clusters/tetrads*_ and has the _*MecA*_ gene) however _*vancomycin*_ is a common initial drug for empiric therapy in hospitalized patients with severe or critical infections.

*Clindamycin*, _*doxycycline*_, and _*SMX/TMP*_ provide important oral options for community-acquired MRSA infections.

The drug of choice for *Stenotrophomonas maltophilia* (which is a _*non-fermenting*_ Gram _*negative*_ _*rod*_) is _*SMX/TMP*_.

A second-line drug for *Stenotrophomonas maltophilia* is _*levofloxacin*_.

The drug of choice for *Nocardia* spp (which is a weakly staining Gram _*positive*_ _*rod*_) is _*SMX/TMP*_.

The drug of choice for *Aspergillus* spp (a type of _*mold*_) is _*voriconazole*_.

*Fluconazole* is generally considered the go-to drug for infections caused by *Candida* spp (which are yeasts). Beware _*fluconazole*_-resistant *Candida* _*glabrata*_, *Candida* _*krusei*_, or *Candida* _*auris*_.

Bugs & Drugs Master Test

Question #1
Which of the following has activity against methicillin-resistant *Staphylococcus aureus* (MRSA)?
A. Cefazolin
B. Cefepime
C. Piperacillin-tazobactam
D. Vancomycin
E. Meropenem

Question #2
Which of the following has activity against Gram negative rod *Pseudomonas aeruginosa*?
A. Ceftriaxone
B. Moxifloxacin
C. Tigecycline
D. Aztreonam
E. Vancomycin

Question #3
Which of the following are known as "respiratory fluoroquinolones" for their ability to work against *Streptococcus pneumoniae*? [select all correct answers]
A. Levofloxacin
B. Ciprofloxacin
C. Moxifloxacin
D. Azithromycin

Question #4
Under which circumstance is nitrofurantoin a potential option for a urinary tract infection? [select all correct answers]
A. Infecting organism is *E. coli*
B. Infecting organism is *Pseudomonas aeruginosa*
C. Infecting organism is *Klebsiella pneumoniae*
D. Infecting organism is *Proteus mirabilis*

Question #5
Which of the following organisms is penicillin likely to be an option for? [select all correct answers]
A. *Treponema pallidum* (Syphilis)
B. *Streptococcus pyogenes* (flesh eating bacteria)
C. *Clostridium perfringens* (gas gangrene)
D. methicillin-sensitive *Staphylococcus aureus* (MSSA)

Question #6
The aminopenicillins (ampicillin and amoxicillin) are widely considered the drugs of choice for which organism? [select all correct answers]
A. *Corynebacterium jeikeium*
B. *Listeria monocytogenes*
C. *Enterococcus faecium*
D. *Clostridioides difficile*

Question #7
What organism are the penicillinase-resistant penicillins (*e.g.*, oxacillin, dicloxacillin) commonly used to treat?
A. *E. coli*
B. Methicillin-sensitive *Staphylococcus aureus* (MSSA)
C. *Haemophilus influenzae*
D. *Streptococcus agalactiae*

Question #8
Which of the following does piperacillin-tazobactam (Zosyn) have activity against, but ampicillin-sulbactam (Unasyn) does not?
A. Methicillin-sensitive *Staphylococcus aureus* (MSSA)
B. Methicillin-resistant *Staphylococcus aureus* (MRSA)
C. *Enterococcus faecalis*
D. *Pseudomonas aeruginosa*

Question #9
Which of the following is true when comparing the activity of piperacillin-tazobactam (Zosyn) to the activity of cefepime (Maxipime)? [select all correct answers]
A. Pip/taz covers *Pseudomonas aeruginosa* and cefepime does not
B. Pip/taz covers *Enterococcus faecalis* and cefepime does not
C. Pip/taz covers *Bacteroides fragilis* and cefepime does not
D. Pip/taz covers methicillin-sensitive *Staphylococcus aureus* (MSSA) and cefepime does not

Question #10
Which of the following is a Gram negative bacteria that cefazolin has activity against? [select all correct answers]
A. *Proteus mirabilis*
B. *E. coli*
C. *Klebsiella pneumoniae*
D. Methicillin-sensitive *Staphylococcus aureus*

Question #11
The cephamycins, cefoxitin and cefotetan, are noteworthy compared to the entire cephalosporin class for which type of antibacterial coverage?
A. Anti-Gram negative activity
B. Anti-Gram positive activity
C. Anti-anaerobic activity
D. Anti-aerobic activity

Question #12
Which of the following is a third-generation cephalosporin with activity against *Pseudomonas aeruginosa*?
A. Ceftazidime
B. Ceftriaxone
C. Cefixime
D. Cefepime

Question #13
Which of the following has activity against methicillin-resistant *Staphylococcus aureus* (MRSA)?
A. Ceftaroline (Teflaro)
B. Ceftazidime-avibactam (Avycaz)
C. Ceftolozane-tazobactam (Zerbaxa)
D. Cefepime

Question #14
Which of the following carbapenems does not have activity against *Pseudomonas aeruginosa*?
A. Meropenem (Merrem)
B. Imipenem-cilastatin (Primaxin)
C. Ertapenem (Invanz)
D. Doripenem (Doribax)
E. Aztreonam (Azactam)

Question #15
Which of the following is widely considered one of the drugs of choice for *E. coli* that produces extended-spectrum beta-lactamases (*i.e.,* is ESBL-positive)?
A. Aztreonam
B. Cefepime
C. Piperacillin-tazobactam
D. Ertapenem

Question #16
Which of the following drug classes has good coverage against atypical organisms (*e.g., Mycoplasma, Legionella, Chlamydia*)? [select all correct answers]
A. Macrolides
B. Penicillins
C. Fluoroquinolones
D. Glycopeptides

Question #17
Which of the following fluoroquinolones is a poor choice for *Pseudomonas aeruginosa*?
A. Levofloxacin
B. Ciprofloxacin
C. Moxifloxacin

Question #18
Which one of the following fluoroquinolones has activity against *Bacteroides fragilis*?
A. Levofloxacin
B. Ciprofloxacin
C. Moxifloxacin

Question #19
Which of the following has activity against Gram negative anaerobe *Bacteroides fragilis*? [select all correct answers]
A. Tigecycline
B. Piperacillin-tazobactam
C. Ertapenem
D. Cefepime
E. Cefoxitin

Question #20
Which of the following is an option for treating Gram positive anaerobe *Clostridioides* [formerly *Clostridium*] *difficile*?
A. Metronidazole
B. Clindamycin
C. Vancomycin (oral route)
D. Vancomycin (IV route)
E. Fidaxomicin

Question #21
Which one of the following macrolides is commonly combined with other drugs (*e.g.,* a proton pump inhibitor plus amoxicillin or metronidazole) to treat infection due to *Helicobacter pylori*?
A. Erythromycin
B. Clarithromycin
C. Azithromycin
D. Clindamycin

Question #22
Which of the following organisms is sulfamethoxazole-trimethoprim (Bactrim, Septra) active against? [select all correct answers]
A. *E. coli*
B. *Stenotrophomonas maltophilia*
C. *Nocardia* spp.
D. Methicillin-resistant *Staphylococcus aureus* (MRSA)
E. Mycobacterium avid complex (MAC)

Question #23
Which of the following has activity against vancomycin-resistant Enterococci (VRE)? [select all correct answers]
A. Daptomycin
B. Linezolid
C. Aztreonam
D. Tigecycline
E. Colistin (aka polymyxin E)

Question #24
Which of the following is an option for treatment of sexually transmitted infection caused by *Chlamydia trachomatis*? [select all correct answers]
A. Ceftriaxone
B. Azithromycin
C. Doxycycline
D. Metronidazole

Question #25
Which of the following is an option for treatment of sexually transmitted infection caused by *Neisseria gonorrhoeae*? [select all correct answers]
A. Ceftriaxone
B. Cefixime
C. Metronidazole
D. Amoxicillin

Question #26
Which of the following drugs is an option for a bite wound where *Pasturella multocida* is a bacteria of concern?
A. Ampicillin
B. Penicillin
C. Cephalexin
D. Amoxicillin-clavulanic acid

Question #27
What is the only organism fidaxomicin is indicated to treat?
A. *Pseudomonas aeruginosa*
B. *Streptococcus pneumoniae*
C. Methicillin-resistant *Staphylococcus aureus* (MRSA)
D. *Clostridioides* [formerly *Clostridium*] *difficile*

Question #28
Glycopeptides are active against Gram negative organisms.
A. True
B. False

Question #29
Which of the following is a common empiric regimen for treatment of *Mycobacterium tuberculosis* infection?
A. Rifampin + isoniazid + pyrazinamide + ethambutol
B. Rifampin + isoniazid + pyrimethamine + ethambutol
C. Ribavirin + isoniazid + pyrazinamide + ethambutol
D. Rifampin + isoniazid + pyrazinamide + erythromycin

Question #30
Which of the following may be used for the treatment or prophylaxis of *Plasmodium* spp. (aka malaria)? [select all correct answers]
A. Chloroquine
B. Atovaquone + proguanil
C. Mefloquine
D. Artesunate
E. Primaquine

Question #31
Which of the following has activity against *Pseudomonas aeruginosa, Mycobacterium tuberculosis* and methicillin-resistant *Staphylococcus aureus* (MRSA)?
A. Linezolid
B. Colistin (polymyxin E)
C. Rifampin
D. Metronidazole

Question #32
Which of the following organisms can fosfomycin be used against? [select all correct answers]
A. *E. coli* that is extended-spectrum beta-lactamase positive (ESBL+)
B. *Morganella morganii*
C. *Bacteroides fragilis*
D. Vancomycin-resistant Enterococci (VRE)
E. Methicillin-resistant *Staphylococcus aureus* (MRSA)

Question #33
Which of the following organisms is methenamine active against?
A. *Klebsiella pneumoniae*
B. *Proteus mirabilis*
C. *E. coli*
D. *Staphylococcus saprophyticus*
E. All listed answers are correct

Question #34
Which one of the following organisms is fluconazole not an option for?
A. *Candida albicans*
B. *Candida krusei* (now also called *Pichia kudriavzevii)*
C. *Candida glabrata*
D. *Candida tropicalis*

Question #35
Which of the following has anti-fungal activity? [select all correct answers]
A. Posaconazole
B. Isavuconazole
C. Metronidazole
D. Albendazole
E. Voriconazole

Question #36
Which of the following organisms do echinocandins (*i.e.*, anidulafungin, micafungin, caspofungin) have activity against?
A. *Candida albicans*
B. *Candida krusei* (now also called *Pichia kudriavzevii*)
C. *Candida glabrata*
D. All listed answers are correct

Question #37
Which of the following is widely considered the drug of choice against *Aspergillus* species?
A. Amphotericin B
B. Voriconazole
C. Anidulafungin
D. Flucytosine

Question #38
Flucytosine is most commonly employed in the treatment of which organism?
A. *Candida albicans*
B. *Mucor* spp.
C. *Candida glabrata*
D. *Cryptococcus neoformans*

Question #39
Which of the following drugs is commonly used for cytomegalovirus (CMV)?
A. Oseltamivir
B. Amantadine
C. Valganciclovir
D. Valacyclovir

Question #40
Which of the following drugs is commonly used against herpes simplex virus (HSV)-1 and HSV-2?
A. Oseltamivir
B. Amantadine
C. Ganciclovir
D. Acyclovir

Question #41
Which of the following can be used against the influenza virus? [select all correct answers]
A. Oseltamivir
B. Peramivir
C. Zanamivir
D. Rimantadine
E. Valganciclovir
F. Baloxavir marboxil

Question #42
Which one of the following is used to treat respiratory syncytial virus (RSV)?
A. Rimantadine
B. Valacyclovir
C. Ribavirin
D. Ledipasvir/sofosbuvir

Question #43
Which of the following can be used in the treatment of hepatitis C? [select all correct answers]
A. Ledipasvir/sofosbuvir
B. Sofosbuvir/velpatasvir
C. Ribavirin
D. Darunavir/cobicistat
E. Elbasvir/grazoprevir

Question #44
Which organism is atovaquone (Mepron) an option for? [select all correct answers]
A. *Cryptococcus gatii*
B. *Toxoplasma gondii*
C. Cytomegalovirus
D. *Pneumocystis jirovecii*

Question #45
Which of the following organisms can sulfadiazine be used to treat?
A. *Cryptococcus gatii*
B. *Toxoplasma gondii*
C. Cytomegalovirus
D. *Pneumocystis jirovecii*

Question #46
Which organism is dapsone an option for? [select all correct answers]
A. *Mycobacterium leprae*
B. *Pneumocystis jirovecii*
C. *Pseudomonas aeruginosa*
D. *Streptococcus pyogenes*

Question #47
Which of the following organisms is ivermectin an option for? [select all correct answers]
A. *Stongyloides stercoralis*
B. *Sarcoptes scabiei*
C. *Gnathostoma spinigerum*
D. *Toxoplasma gondii*

Question #48
Which of the following has activity against *Salmonella* species? [select all correct answers]
A. Ciprofloxacin
B. Metronidazole
C. Sulfamethoxazole-trimethoprim
D. Ampicillin

Question #49
Which of the following is widely regarded as the drug of choice for treatment of *Borreliella* (formerly *Borrelia*)*burgdorferi* (Lyme Disease)?
A. Sulfamethoxazole-trimethoprim
B. Doxycycline
C. Clindamycin
D. Linezolid

Question #50
Which of the following organisms can nitazoxanide (Alinia) be used to treat?
A. *Cryptosporidium parvum*
B. *Giardia lambia*
C. *Pseudomonas aeruginosa*
D. *Toxoplasma gondii*

ANSWERS

Question #1 Explanations:
Which of the following has activity against methicillin-resistant *Staphylococcus aureus* (MRSA)?
NOTE: Carbapenems (ertapenem, imipenem-cilastatin, meropenem, doripenem) are broad spectrum and can be used against many drug-resistant Gram negative infections, but they lack activity against drug-resistant Gram positive organisms such as MRSA.
A. Cefazolin - **INCORRECT: can cover MSSA but not MRSA**
B. Cefepime - **INCORRECT: can cover MSSA but not MRSA**
C. Piperacillin-tazobactam - **INCORRECT: can cover MSSA but not MRSA**
D. Vancomycin - **CORRECT: can have activity against MRSA**
E. Meropenem - **INCORRECT: can cover MSSA but not MRSA**

Question #2 explained:
Which of the following has activity against Gram negative rod *Pseudomonas aeruginosa*?
A. Ceftriaxone - **INCORRECT: will cover many Gram negatives but unlike ceftazidime this third-generation cephalosporin lacks *Pseudomonas* coverage**
B. Moxifloxacin - **INCORRECT: unlike ciprofloxacin and levofloxacin, this fluoroquinolone lacks *Pseudomonas* coverage**
C. Tigecycline - **INCORRECT: while tigecycline covers many organisms (*e.g.*, VRE, MRSA, ESBLs, CRE), *Pseudomonas* is the major hole in its spectrum of activity**
D. Aztreonam - **CORRECT: this monobactam is frequently over-looked, but with only Gram negative activity, it can be an option for *Pseudomonas***
E. Vancomycin - **INCORRECT: vancomycin only has Gram positive activity (just like daptomycin and telavancin) and *Pseudomonas* is a Gram negative bacteria**

Question #3 explained:
Which of the following are known as "respiratory fluoroquinolones" for their ability to cover *Streptococcus pneumoniae*?
NOTE: Many people believe levofloxacin and moxifloxacin are labeled "respiratory fluoroquinolones" for their ability to penetrate into the lungs. This is incorrect. Ciprofloxacin, moxifloxacin and levofloxacin all achieve good lung penetration. The difference is ciprofloxacin does not have good activity against *Streptococcus pneumoniae*. The newer fluoroquinolone delafloxacin (Baxdela) has activity against *Strep. pneumoniae*.
A. Levofloxacin - **CORRECT**
B. Ciprofloxacin - **INCORRECT**
C. Moxifloxacin - **CORRECT**
D. Azithromycin - **INCORRECT: is not a fluoroquinolone**

Question #4 explained
Under which circumstance is nitrofurantoin a potential option for a urinary tract infection?
NOTE: Nitrofurantoin is only used for treatment of urinary tract infection, which is most commonly caused by Gram negative bacteria *E. coli*. This can help you remember that nitrofurantoin can be used against *E. coli*. It is also active against some *Klebsiella* isolates, but is has little to no role in treating *Pseudomonas* spp. or *Proteus* spp.
A. Infecting organism is *E. coli* - **CORRECT**
B. Infecting organism is *Pseudomonas aeruginosa* - **INCORRECT: nitrofurantoin lacks coverage for this organism**
C. Infecting organism is *Klebsiella pneumoniae* - **CORRECT**
D. Infecting organism is *Proteus mirabilis* - **INCORRECT: nitrofurantoin lacks coverage for this organism**

Question #5 explained
Which of the following organisms is penicillin likely to be an option for?
A. *Treponema pallidum* (Syphilis) - **CORRECT: penicillin is widely considered the drug of choice for syphilis**
B. *Streptococcus pyogenes* (flesh eating bacteria) - **CORRECT: beta-hemolytic Streptococci (*e.g.*, *S. pyogenes* & *S. agalactiae*) are most commonly penicillin sensitive, while alpha-hemolytic Streptococci (*e.g.*, *S. pneumoniae* & Viridans Streptococci) may be resistant**
C. *Clostridium perfringens* (gas gangrene) - **CORRECT: penicillin is widely considered the drug of choice for this organism and may be combined with clindamycin when used for this purpose, because clindamycin helps inhibit toxins**
D. methicillin-sensitive *Staphylococcus aureus* (MSSA) - **INCORRECT: MSSA can be penicillin sensitive, but the vast majority in USA are resistant to penicillin due to penicillinase production**

Question #6 explained
The aminopenicillins (ampicillin and amoxicillin) are widely considered the drugs of choice for which organism?
A. *Corynebacterium jeikeium* - **INCORRECT: vancomycin is widely considered the drug of choice for this organism, but if you see it growing, first rule-out contamination before looking to select a drug for treatment**
B. *Listeria monocytogenes* - **CORRECT**
C. *Enterococcus faecium* - **CORRECT: while *E. faecium* is frequently resistant to both aminopenicillins and vancomycin (making VRE), aminopenicillins are widely considered the drugs of choice for susceptible Enterococci**
D. *Clostridioides difficile* - **INCORRECT: aminopenicillins have no clinical utility against this Gram positive anaerobe**

Question #7 explained
What organism are the penicillinase-resistant penicillins (*e.g.*, oxacillin, dicloxacillin) commonly used to treat?
NOTE: The acronym "CONDOM" is used to help remember this group of drugs: cloxacillin, oxacillin, nafcillin, dicloxacillin, oxacillin, methicillin. The other name for the penicillinase-resistant penicillins is the anti-Staphylococcal penicillins. This is not an acronym to use on rounds, but is helpful for remembering these drugs.
A. *E. coli* - **INCORRECT: these drugs lack Gram negative activity**
B. Methicillin-sensitive *Staphylococcus aureus* (MSSA) - **CORRECT: these drugs are almost exclusively used for MSSA**
C. *Haemophilus influenzae* - **INCORRECT: these drugs lack Gram negative activity**
D. *Streptococcus agalactiae* - **INCORRECT: while they may be active against this Gram positive organism, it is very uncommon to use a penicillinase-resistant penicillin for this organism**

Question #8 explained
Which of the following does piperacillin-tazobactam (Zosyn) have activity against, but ampicillin-sulbactam (Unasyn) does not?
A. Methicillin-sensitive *Staphylococcus aureus* (MSSA) - **INCORRECT: both drugs cover this organism**
B. Methicillin-resistant *Staphylococcus aureus* (MRSA) - **INCORRECT: neither drugs cover this organism**
C. *Enterococcus faecalis* - **INCORRECT: both drugs cover this organism**
D. *Pseudomonas aeruginosa* - **CORRECT: ampicillin-sulbactam lacks activity against this non-fermenting Gram negative rod**

Question #9 explained
Which of the following is true when comparing the activity of piperacillin-tazobactam (Zosyn) to the activity of cefepime (Maxipime)?
A. Pip/taz covers *Pseudomonas aeruginosa* and cefepime does not - **INCORRECT: both drugs have activity against this non-fermenting Gram negative rod**
B. Pip/taz covers *Enterococcus faecalis* and cefepime does not - **CORRECT: note that when cefepime is used with vancomycin, the vancomycin will provide coverage for Enterococcus**
C. Pip/taz covers *Bacteroides fragilis* and cefepime does not - **CORRECT: cefepime lacks any substantial anaerobic coverage**
D. Pip/taz covers methicillin-sensitive *Staphylococcus aureus* (MSSA) and cefepime does not - **INCORRECT: both drugs cover MSSA**

Question #10 explained
Which of the following is a Gram negative bacteria that cefazolin has activity against?
NOTE: The acronym "PEcK" is used to help remember that cefazolin has activity against *Proteus, E. coli, Klebsiella.*
A. *Proteus mirabilis* - **CORRECT**
B. *E. coli* - **CORRECT**
C. *Klebsiella pneumoniae* - **CORRECT**
D. Methicillin-sensitive *Staphylococcus aureus* - **INCORRECT: while cefazolin is active against this bacteria, this bug is Gram positive not Gram negative**

Question #11 explained
The cephamycins, cefoxitin and cefotetan, are noteworthy compared to the entire cephalosporin class for which type of antibacterial coverage?
NOTE: The term "tan fox" is used to help remember cefotetan and cefoxitin. Beware that while they do have notable anti-anaerobic activity, resistance with Gram negative anaerobe *Bacteroides fragilis* can be an issue. As a general rule, none of the cephalosporins (outside the cephamycins) have good anti-anaerobic activity.
A. Anti-Gram negative activity - **INCORRECT**
B. Anti-Gram positive activity - **INCORRECT**
C. Anti-anaerobic activity - **CORRECT**
D. Anti-aerobic activity - **INCORRECT**

Question #12 explained
Which of the following is a third-generation cephalosporin with activity against *Pseudomonas aeruginosa*?
A. Ceftazidime - **CORRECT**
B. Ceftriaxone - **INCORRECT: this third-generation cephalosporin lacks coverage for *Pseudomonas aeruginosa***
C. Cefixime - **INCORRECT: this third-generation cephalosporin lacks coverage for *Pseudomonas aeruginosa***
D. Cefepime - **INCORRECT: this is a fourth-generation cephalosporin**

Question #13 explained
Which of the following has activity against methicillin-resistant *Staphylococcus aureus* (MRSA)?
NOTE: All listed answers have activity against methicillin-sensitive *Staphylococcus aureus* (MSSA).
A. Ceftaroline (Teflaro) - **CORRECT: this is the only beta-lactam in the United States with anti-MRSA activity**
B. Ceftazidime-avibactam (Avycaz) - **INCORRECT: this drug can cover carbapenem-resistant *Klebsiella pneumoniae*, but not MRSA**
C. Ceftolozane-tazobactam (Zerbaxa) - **INCORRECT: this drug can cover carbapenem-resistant *Pseudomonas aeruginosa*, but not MRSA**
D. Cefepime - **INCORRECT: this drugs covers *Pseudomonas aeruginosa*, but not MRSA**

Question #14 explained
Which of the following carbapenems does not have activity against *Pseudomonas aeruginosa*?
NOTE: Ertapenem is informally known as "monkey-cillin" because it lacks activity against "APE" - Acinetobacter,Pseudomonas, and Enterococcus species.
A. Meropenem (Merrem) - **INCORRECT**
B. Imipenem-cilastatin (Primaxin) - **INCORRECT**
C. Ertapenem (Invanz) - **CORRECT**
D. Doripenem (Doribax) - **INCORRECT**
E. Aztreonam (Azactam) - **INCORRECT: has activity versus Pseudomonas but it is not a carbapenem; aztreonam is a monobactam**

Question #15 explained
Which of the following is widely considered one of the drugs of choice for *E. coli* that produces extended-spectrum beta-lactamases (*i.e.,* is ESBL-positive)?
NOTE: Carbapenems are widely considered the drugs of choice for infection caused by an ESBL-producing organism. The role of aztreonam, cefepime and piperacillin-tazobactam for ESBLs is a heavily debated topic.
A. Aztreonam - **INCORRECT**
B. Cefepime - **INCORRECT**
C. Piperacillin-tazobactam - **INCORRECT**
D. Ertapenem - **CORRECT**

Question #16 explained
Which of the following drug classes has good coverage against atypical organisms (*e.g., Mycoplasma, Legionella, Chlamydia*)?
NOTE: tetracyclines are also a class to consider when coverage for atypical organisms is needed.
A. Macrolides - **CORRECT**
B. Penicillins - **INCORRECT**
C. Fluoroquinolones - **CORRECT**
D. Glycopeptides - **INCORRECT**

Question #17 explained
Which of the following fluoroquinolones is a poor choice for *Pseudomonas aeruginosa*?
NOTE: Ciprofloxacin and levofloxacin are options for *Pseudomonas* , whereas moxifloxacin does not have activity against this organism.
A. Levofloxacin - **INCORRECT**
B. Ciprofloxacin - **INCORRECT**
C. Moxifloxacin - **CORRECT**

Question #18 explained
Which one of the following fluoroquinolones has activity against *Bacteroides fragilis*?
NOTE: Moxifloxacin has the added capacity to cover the Gram negative anaerobe *Bacteroides fragilis*. This organism can be resistant to moxifloxacin, so beware when using in clinical practice. The anti-anaerobic activity of moxifloxacin makes it special as compared to other fluoroquinolones.
A. Levofloxacin - **INCORRECT**
B. Ciprofloxacin - **INCORRECT**
C. Moxifloxacin - **CORRECT**

Question #19 explained
Which of the following has activity against Gram negative anaerobe *Bacteroides fragilis*?
NOTE: This one is pretty straight-forward. When it comes to anaerobic bacteria, this is the big Gram negative one to know about. Metronidazole is another drug to consider for this organism.
A. Tigecycline - **CORRECT**
B. Piperacillin-tazobactam - **CORRECT**
C. Ertapenem - **CORRECT**
D. Cefepime - **INCORRECT**
E. Cefoxitin - **CORRECT**

Question #20 explained
Which of the following is an option for treating Gram positive anaerobe *Clostridioides* [formerly *Clostridium*] *difficile*?
A. Metronidazole - **CORRECT (although it has largely fallen out of favor, see IDSA C. difficile guidelines)**
B. Clindamycin - **INCORRECT: this drug is one of the most common to be implicated in causing *C. difficile* infection. It's potent anti-anaerobic activity kills off the bacteria *C. difficile* competes with, but not *C. difficile*, thus creating the opportunity for *C. difficile* to proliferate and cause infection.**
C. Vancomycin (oral route) - **CORRECT**
D. Vancomycin (IV route) - **INCORRECT: while vancomycin oral is not well absorbed and stays in the gut to work on where *C. difficile* is causing infection, the IV route vancomycin will not get to there and will not treat it.**
E. Fidaxomicin - **CORRECT**

Question #21 explained
Which one of the following macrolides is commonly combined with other drugs (*e.g.*, a proton pump inhibitor plus amoxicillin or metronidazole) to treat infection due to *Helicobacter pylori*?
NOTE: Previous macrolide exposure or residence in an area where macrolide resistance in *H. pylori* is known to be high may preclude the use of clarithromycin.
A. Erythromycin - **INCORRECT**
B. Clarithromycin - **CORRECT**
C. Azithromycin - **INCORRECT**
D. Clindamycin - **INCORRECT: is a lincosamide, not a macrolide and is not used for this organism**

Question #22 explained
Which of the following organisms is sulfamethoxazole-trimethoprim (Bactrim, Septra) active against?
A. *E. coli* - **CORRECT: SMX/TMP is widely used for urinary tract infection caused by *E. coli*, but beware increasing prevalence of resistance**
B. *Stenotrophomonas maltophilia* - **CORRECT: this organism can be resistant to SMX/TMP, but this drug is widely considered first-line against the non-fermenting Gram negative rod *S. maltophilia***
C. *Nocardia* spp. - **CORRECT: there are many species of Nocardia and resistance patterns vary by species, however SMX/TMP is widely considered a first-line drug for these organisms**
D. Methicillin-resistant *Staphylococcus aureus* (MRSA) - **CORRECT: community-acquired MRSA is commonly susceptible to SMX/TMP and clindamycin too, whereas resistance to SMX/TMP and clindamycin in healthcare-associated MRSA is common**
E. Mycobacterium avid complex (MAC) - **INCORRECT: while SMX/TMP is a go-to option for opportunistic infections caused by PCP and toxoplasma, it is not effective for MAC. Preferred therapy for MAC treatment is azithromycin or clarithromycin plus ethambutol.**

Question #23 explained
Which of the following has activity against vancomycin-resistant Enterococci (VRE)?
NOTE: The optimal therapy for VRE is not known, but linezolid, daptomycin and tigecycline are the most common drugs to consider. Quinupristin/ dalfopristin can also have VRE activity, but this drug is rarely used because of its extensive toxicities.
A. Daptomycin - **CORRECT**
B. Linezolid - **CORRECT**
C. Aztreonam - **INCORRECT: aztreonam only has Gram negative activity and Enterococci are Gram positive bacteria**
D. Tigecycline - **CORRECT**
E. Colistin (aka polymyxin E) - **INCORRECT: colistin only has Gram negative activity and Enterococci are Gram positive**

Question #24 explained
Which of the following is an option for treatment of sexually transmitted infection caused by *Chlamydia trachomatis*?
NOTE: Alternative options for *C. trachomatis* include erythromycin and levofloxacin.
A. Ceftriaxone - **INCORRECT: ceftriaxone monotherapy is not indicated for *C. trachomatis***
B. Azithromycin - **CORRECT: usually given as a single 1gm dose**
C. Doxycycline - **CORRECT: usually given as 100mg twice daily for 7 days**
D. Metronidazole - **INCORRECT: is not active against this organism**

Question #25 explained
Which of the following is an option for treatment of sexually transmitted infection caused by *Neisseria gonorrhoeae*?
NOTE: Ceftriaxone is first-line as per 2021 CDC STI Treatment Guidelines. Cefixime can be used as an alternative agent to treat uncomplicated gonococcal infection of the cervix, urethra, or rectum in adults and adolescents, but it must be combined with gentamicin. Resistance to *N. gonorrhoeae* is a worldwide concern, even being resistant to all conventional therapies at times, yikes!
A. Ceftriaxone - **CORRECT**
B. Cefixime - **CORRECT**
C. Metronidazole - **INCORRECT: is not active against this organism**
D. Amoxicillin - **INCORRECT: it is uncommon for this organism to be sensitive to penicillins and thus this aminopenicillin is not an option**

Question #26 explained
Which of the following drugs is an option for a bite wound where *Pasturella multocida* is a bacteria of concern?
NOTE: *Pasturella multocida* is a facultative anaerobic Gram negative bacterium that produces penicillinases which render most penicillins ineffective. It is commonly a concern with bite wounds. Addition of a beta-lactamase inhibitor (*i.e.*, clavulanic acid or sulbactam) expands coverage of aminopenicillins (*i.e.*, amoxicillin or ampicillin) to include this organism.
A. Ampicillin - **INCORRECT**
B. Penicillin - **INCORRECT**
C. Cephalexin - **INCORRECT: like all cephalosporins, this drug is largely ineffective against anaerobic organisms**
D. Amoxicillin-clavulanic acid - **CORRECT: is generally considered the first-line drug for both human or animal bite wounds**

Question #27 explained
What is the only organism fidaxomicin is indicated to treat?
NOTE: Fidaxomicin (Dificid) has a limited antimicrobial spectra and specifically targets *C. difficile*. The lack of broad-spectrum activity provides less "collateral damage" as compared to other options and is meant to help preserve the patients existing microbiome. The other two major drugs to consider for *C. difficile* are metronidazole (less so) and oral or rectal route vancomycin. Bezoltoxumab (Zinplava) is indicated for prevention of *C. difficile*. Bezlotoxumab and fidaxomicin are both expensive.
A. *Pseudomonas aeruginosa* - **INCORRECT**
B. *Streptococcus pneumoniae* - **INCORRECT**
C. methicillin-resistant *Staphylococcus aureus* (MRSA) - **INCORRECT**
D. *Clostridioides* [formerly *Clostridium*] *difficile* - **CORRECT**

Question #28 explained
Glycopeptides are active against Gram negative organisms.
NOTE: Glycopeptides such as vancomycin, daptomycin, telavancin, oritavancin and dalbavancin are all nearly exclusively active against Gram positive organisms only (e.g., Staphylococci, Streptococci, Enterococci).
A. True - **INCORRECT**
B. False - **CORRECT**

Question #29 explained
Which of the following is a common empiric regimen for treatment of *Mycobacterium tuberculosis* infection?
NOTE: The acronym "RIPPE" is commonly used to help remember the common treatment of tuberculosis (answer A). The second "P" is for pyridoxine (aka vitamin B6), which helps minimize toxicity from isoniazid.
A. Rifampin + isoniazid + pyrazinamide + ethambutol - **CORRECT**
B. Rifampin + isoniazid + pyrimethamine + ethambutol - **INCORRECT: be careful not to confuse pyrimethamine with pyrazinamide. Pyrimethamine can be used for treating PCP or toxoplasmosis (amongst other organisms).**
C. Ribavirin + isoniazid + pyrazinamide + ethambutol - **INCORRECT: ribavirin is a common drug used in the treatment of hepatitis C, not tuberculosis**
D. Rifampin + isoniazid + pyrazinamide + erythromycin - **INCORRECT: ethambutol not erythromycin is a first-line drug for tuberculosis**

Question #30 explained
Which of the following may be used for the treatment or prophylaxis of *Plasmodium* spp. (aka malaria)?
NOTE: You may be surprised that all answers listed were correct and it is likely you have never heard of artesunate (an IV anti-malarial). This question is meant to help show there are many options for malaria and these are some of the most frequently employed drugs (with the exception of artesunate). There are several different plasmodium species that cause malaria and resistance patterns vary across both species and geographic regions. Doxycycline can also have activity against malaria.
A. Chloroquine - **CORRECT**
B. Atovaquone + proguanil - **CORRECT: brand name Malarone**
C. Mefloquine - **CORRECT**
D. Artesunate - **CORRECT**
E. Primaquine - **CORRECT: commonly combined with chloroquine or hydroxychloroquine for treatment of malaria**

Question #31 explained
Which of the following has activity against *Pseudomonas aeruginosa*, *Mycobacterium tuberculosis* and methicillin-resistant *Staphylococcus aureus* (MRSA)?
NOTE: Rifampin is limited in that it is rarely indicated as monotherapy, but rifampin has an extremely broad spectrum activity.
A. Linezolid - **INCORRECT: does not cover *Pseudomonas aeruginosa***
B. Colistin (polymyxin E) - **INCORRECT: does not cover MRSA or tuberculosis**
C. Rifampin - **CORRECT**
D. Metronidazole - **INCORRECT: does not cover any of the listed organisms**

Question #32 explained
Which of the following organisms can fosfomycin be used against?
NOTE: In the United States fosfomycin is only available oral for the treatment of urinary tract infection (UTI), but in other countries it is available as injectable and used for a variety of indications. *E. coli* is the leading cause of UTI, which can help you remember fosfomycin works against this organism since it is a "UTI drug."
A. *E. coli* that is extended-spectrum beta-lactamase positive (ESBL+) - **CORRECT**
B. *Morganella morganii* - **INCORRECT: this is one of the few organisms fosfomycin is not active against**
C. *Bacteroides fragilis* - **INCORRECT: this is one of the few organisms fosfomycin is not active against**
D. Vancomycin-resistant Enterococci (VRE) - **CORRECT**
E. Methicillin-resistant *Staphylococcus aureus* (MRSA) - **CORRECT**

Question #33 explained
Which of the following organisms is methenamine active against?
NOTE: Methenamine is a urinary tract antiseptic. When the urine is acidic methenamine converts into formaldehyde, which exerts an antimicrobial effect against the majority of microorganisms. It can be more of a challenge to achieve acidic urine in patients colonized with *Proteus* or *Pseudomonas*, which can be urea-splitting and increase pH. Methenamine is only used for UTI prevention, not UTI treatment. Patients must retain urine in their bladder to allow methenamine to work, so it is not an option for people with chronic urinary catheters who do not retain urine in their bladder.
A. *Klebsiella pneumoniae* - **TRUE, BUT WRONG ANSWER**
B. *Proteus mirabilis*- **TRUE, BUT WRONG ANSWER**
C. *E. coli* - **TRUE, BUT WRONG ANSWER**
D. *Staphylococcus saprophyticus* - **TRUE, BUT WRONG ANSWER**
E. All listed answers are correct- **CORRECT**

Question #34 explained
Which one of the following organisms is fluconazole not an option for?
NOTE: Fluconazole is generally considered the go-to drug for infections caused by *Candida* species, but beware *C. krusei* is resistant to fluconazole. *C. glabrata* can be resistant to fluconazole at times. Fluconazole resistance in *C. albicans* or *C. tropicalis* is extremely uncommon. *C. auris* is another yeast to beware resistance in.
A. *Candida albicans* - **INCORRECT**
B. *Candida krusei* (now also called *Pichia kudriavzevii*) - **CORRECT**
C. *Candida glabrata* - **INCORRECT**
D. *Candida tropicalis* - **INCORRECT**

Question #35 explained
Which of the following has anti-fungal activity?
NOTE: Just because it ends in "azole" does not necessarily mean it is an "Azole anti-fungal." Even the PPI's end in azole! (e.g., pantoprazole)
A. Posaconazole- **CORRECT**
B. Isavuconazole- **CORRECT**
C. Metronidazole- **INCORRECT: has activity against many infectious pathogens, but not fungi**
D. Albendazole- **INCORRECT: is an anti-helmintic medication (works against worms and other parasites), but does not have anti-fungal activity**
E. Voriconazole- **CORRECT**

Question #36 explained
Which of the following organisms do echinocandins (*i.e.*, anidulafungin, micafungin, caspofungin) have activity against?
NOTE: Echinocandins are a common go-to class for when a possible fluconazole-resistant Candida species is suspected, because of their broad spectrum of activity which covers most Candida species. *Candida parapsilosis* can have higher MICs versus echinocandins but the clinical relevance of this is not clear. Beware echinocandin resistance in *Candida auris*.
A. *Candida albicans* - **TRUE, BUT WRONG ANSWER**
B. *Candida krusei* (now also called *Pichia kudriavzevii*) - **TRUE, BUT WRONG ANSWER**
C. *Candida glabrata* - **TRUE, BUT WRONG ANSWER**
D. All listed answers are correct - **CORRECT**

Question #37 explained
Which of the following is widely considered the drug of choice against *Aspergillus* species?
A. Amphotericin B- **INCORRECT: is a broad-spectrum anti-fungal that will cover many *Aspergillus* spp., but is not considered the drug of choice for this group of organisms**
B. Voriconazole- **CORRECT**
C. Anidulafungin- **INCORRECT: is sometimes used as part of a salvage regimen for these organisms, but is not considered a first-line agent**
D. Flucytosine- **INCORRECT: would be extremely uncommon to use this drug for treating *Aspergillus* spp.**

Question #38 explained
Flucytosine is most commonly employed in the treatment of which organism?
NOTE: Flucytosine is most commonly used in treating infection caused by opportunistic pathogen *Cryptococcal neoformans*, which is known for causing meningitis in HIV/AIDS patients. Flucytosine is typically combined with amphotericin B for this purpose. Flucytosine has activity against some *Candida* spp., but it is not common to use this drug for that purpose. Do not use flucytosine as monotherapy because resistance can develop during treatment.
A. *Candida albicans*- **INCORRECT**
B. *Mucor* spp. - **INCORRECT**
C. *Candida glabrata*- **INCORRECT**
D. *Cryptococcus neoformans*- **CORRECT**

Question #39 explained
Which of the following drugs is commonly used for cytomegalovirus (CMV)?
A. Oseltamivir - **INCORRECT: used against influenza**
B. Amantadine - **INCORRECT: used against influenza A, although not commonly due to resistance issues**
C. Valganciclovir - **CORRECT: the IV counterpart to valganciclovir is ganciclovir. Ganciclovir also comes as oral but valganciclovir (Valcyte) is generally the preferred oral anti-CMV drug.**
D. Valacyclovir - **INCORRECT: be careful not to confuse this drug that is used for herpes simplex virus 1 and 2 with the drug valganciclovir, as their names are quite similar**

Question #40 explained
Which of the following drugs is commonly used against herpes simplex virus (HSV)-1 and HSV-2?
A. Oseltamivir- **INCORRECT: used against influenza viruses**
B. Amantadine- **INCORRECT: used against influenza A, although not commonly due to resistance issues**
C. Ganciclovir- **INCORRECT: most commonly used against CMV**
D. Acyclovir- **CORRECT: acyclovir is similar to valacyclovir (Valtrex) and either can be used against HSV-1 or HSV-2. Acyclovir comes as an injectable formulation while valacyclovir does not.**

Question #41 explained
Which of the following can be used against the influenza virus?
NOTE: Oseltamivir (Tamiflu), peramivir (Rapivab) and zanamivir (Relenza) are neuraminidase inhibitors with activity against some influenza virus strains. Baloxavir marboxil (Xofluza) polymerase acidic endonuclease inhibitor that is only used for influenza. Amantadine can be active against influenza A, but it is not used much any more due to resistance issues.
A. Oseltamivir- **CORRECT**
B. Peramivir- **CORRECT**
C. Zanamivir- **CORRECT**
D. Rimantadine- **CORRECT**
E. Valganciclovir- **INCORRECT: is used for CMV not influenza**
F. Baloxavir marboxil- **CORRECT**

Question #42 explained
Which one of the following is used to treat respiratory syncytial virus (RSV)?
A. Rimantadine- **INCORRECT: can be used for influenza A, but resistance is an issue**
B. Valacyclovir- **INCORRECT: used for HSV-1 and HSV-2**
C. Ribavirin- **CORRECT: ribavirin is the most common drug used to treat RSV, which is most frequently seen causing infection in pediatric patients.**
D. Ledipasvir/sofosbuvir- **INCORRECT: used for hepatitis C**

Question #43 explained
Which of the following can be used in the treatment of hepatitis C?
A. Ledipasvir/sofosbuvir (Harvoni) - **CORRECT**
B. Sofosbuvir/velpatasvir (Epclusa) - **CORRECT**
C. Ribavirin - **CORRECT: can be used to treat hepatitis C, however should be used as a part of combination therapy**
D. Darunavir/cobicistat (Prezcobix) - **INCORRECT: is for treatment of HIV**
E. Elbasvir/grazoprevir (Zepatier) - **CORRECT**

Question #44 explained
Which organism is atovaquone (Mepron) an option for?
NOTE: All of these organisms listed are known to cause infection in HIV/AIDS patients. The most common reason to use atovaquone is for PCP in a patient with sulfa allergy (i.e., when sulfamethoxazole-trimethoprim aka Bactrim aka Septra is not an option).
A. *Cryptococcus gatii* - **INCORRECT: this organism is a fungi (or more specifically a yeast) for which atovaquone is not active**
B. *Toxoplasma gondii* - **CORRECT**
C. Cytomegalovirus - **INCORRECT: this is a virus for which atovaquone is not active**
D. *Pneumocystis jirovecii* - **CORRECT**

Question #45 explained
Which of the following organisms can sulfadiazine be used to treat?
NOTE: Sulfadiazine is commonly combined with pyrimethamine plus leucovorin when treating toxoplasmosis. It can also be combined with atovaquone for this purpose.
A. *Cryptococcus gatii* - **INCORRECT**
B. *Toxoplasma gondii* - **CORRECT**
C. Cytomegalovirus - **INCORRECT**
D. *Pneumocystis jirovecii* - **INCORRECT**

Question #46 explained
Which organism is dapsone an option for?
NOTE: Dapsone is most commonly used as a second or third-line option. It does not have coverage for Gram negative or Gram positive bacteria, but interestingly it can be used to treat leprosy.
A. *Mycobacterium leprae* - **CORRECT**
B. *Pneumocystis jirovecii* - **CORRECT**
C. *Pseudomonas aeruginosa* - **INCORRECT**
D. *Streptococcus pyogenes* - **INCORRECT**

Question #47 explained
Which of the following organisms is ivermectin an option for?
NOTE: Ivermectin (Stromectol) is an anthelmintic medication that can be used to treat parasitic worms and scabies.
A. *Stongyloides stercoralis* - **CORRECT: is a type of worm**
B. *Sarcoptes scabiei* - **CORRECT: is a type of scabies**
C. *Gnathostoma spinigerum* - **CORRECT: is a type of worm**
D. *Toxoplasma gondii* - **INCORRECT: ivermectin does not treat this organism**

Question #48 explained
Which of the following has activity against *Salmonella* species?
NOTE: Drug-resistant Salmonella is on the rise and while the answers noted as correct may have activity, beware resistance in this organism.
A. Ciprofloxacin - **CORRECT**
B. Metronidazole - **INCORRECT**
C. Sulfamethoxazole-trimethoprim - **CORRECT**
D. Ampicillin - **CORRECT**

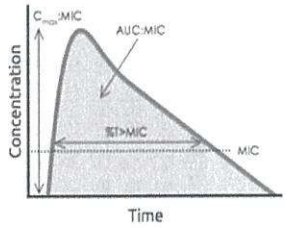
Question #49 explained
Which of the following is widely regarded as the drug of choice for treatment of *Borreliella* (formerly *Borrelia*) *burgdorferi* (Lyme Disease)?
NOTE: While doxycycline is typically the go-to drug for Lyme Disease in adults, amoxicillin is a common go-to drug for Lyme Disease in children due to toxicity concerns with doxycycline in children less than 8 years old. Like syphilis, Lyme disease is a spirochete.
A. Sulfamethoxazole-trimethoprim - **INCORRECT**
B. Doxycycline - **CORRECT**
C. Clindamycin - **INCORRECT**
D. Linezolid - **INCORRECT**

Question #50 explained
Which of the following organisms can nitazoxanide (Alinia) be used to treat?
NOTE: Nitazoxanide is not a commonly used medication, but it is widely considered the drug of choice for Cryptosporidiosis-associated diarrhea. Nitazoxanide also has activity against *Clostridium difficile*, but it's role in treating this organism is not well defined. When you come across this drug it is almost always going to be for treating an organism that causes diarrhea.
A. *Cryptosporidium parvum*- **CORRECT**
B. *Giardia lambia*- **CORRECT**
C. *Pseudomonas aeruginosa*- **INCORRECT**
D. *Toxoplasma gondii*- **INCORRECT**

Beta-Lactams Cheat Sheet

β-LACTAM CLASSES	
β-lactam Class	**Coverage Generalization**
PENICILLINS	
Penicillins: aqueous PCN G, PCN V potassium, PCN benzathine, procaine PCN	Streptococci, basic anaerobes (*e.g.*, non-difficile *Clostridioides* spp), syphilis (*Treponema pallidum*)
Aminopenicillins: ampicillin, amoxicillin	Enterococci (DOC), Streptococci, basic anaerobes, *Listeria monocytogenes* (DOC), not MSSA
Anti-Staphylococcal Penicillins aka Penicillinase-resistant penicillins	"CONDOM" – cloxacillin, oxacillin, nafcillin, dicloxacillin, oxacillin (again), methicillin -A go-to class for MSSA infections
Penicillin/BLI combinations: ampicillin-sulbactam, amoxicillin-clavulanic acid, piperacillin-tazobactam	Streptococci, Enterococci, MSSA, Gram negatives (more with pip/taz, which also has *Pseudomonas* activity), anaerobes (including *Bacteroides fragilis*)
CEPHALOSPORINS (As a class, have limited coverage versus anaerobes & Enterococci)	
1st gen: cephalexin, cefadroxil, cefazolin (IV)	Streptococci, MSSA, "PEcK" – *Proteus, E. coli, Klebsiella*
2nd gen: cefoxitin (IV), cefotetan (IV), cefaclor, cefprozil, cefuroxime (IV)	Streptococci, MSSA, "HEN PEcK" *(Haemophilus influenzae, Neisseria, Proteus, E. coli, Klebsiella*), cefoxitin and cefotetan are cephamycins and have anaerobic activity
I gen: ceftriaxone (IV), ceftazidime (IV), cefdinir, cefixime, cefotaxime, cefpodoxime, ceftibuten	Streptococci (better than 1st or 2nd gen), MSSA (not as good as 1st or 2nd gen), broad gram negative coverage (ceftazidime even has *Pseudomonas* activity)
4th gen: cefepime (IV)	Streptococci (better than 1st or 2nd gen), MSSA, broad Gram negative coverage (better than 3rd gen) and has *Pseudomonas* activity
"5th" gen: ceftaroline (IV)	Like ceftriaxone + MRSA coverage
Cephalosporin/ BLI combinations: Ceftazidime/avibactam (IV), ceftolozane-tazobactam (IV)	MSSA, Streptococci, broad Gram negative coverage including *Pseudomonas* and some carbapenem-resistant bacteria
Siderophore Cefiderocol (IV)	Active versus drug resistant Gram negatives (*e.g.,* Acinetobacter & Pseudomonas)
CARBAPENEMS (All are IV only, all have broad Gram negative activity, and none cover MRSA)	
Carbapenems: ertapenem, meropenem, imipenem-cilastatin, doripenem	MSSA, streptococci, anaerobes (including *B. fragilis*), ertapenem lacks coverage for "APE" – *Acinetobacter, Pseudomonas, Enterococcus*; Considered DOC for ESBL+
Carbapenem/BLI combinations: meropenem-vaborbactam, imipenem-cilastatin-relebactam	Above + some carbapenem-resistant Gram negative organisms; imi-rel can kill some imi-resistant Pseudomonas isolates
MONOBACTAM (not a beta-lactam)	
Monobactam: aztreonam (IV, inhaled)	Gram negative coverage only, including *Pseudomonas aeruginosa*

The PK-PD indices associated with antibacterial activity



β-lactams exhibit time-dependant killing
→ The longer the time above the MIC during the dosing interval, the more killing

Similar side chains	Penicillin	Amoxicillin	Ampicillin	Cephalexin	Cefuroxime	Cefoxitin	Ceftriaxone	Cefotaxime	Cefepime	Ceftazidime
Penicillin	■					X				
Amoxicillin		■	X	X						
Ampicillin		X	■	X						
Cephalexin		X	X	■						
Cefuroxime					■	X	X	X		
Cefoxitin	X				X	■				
Ceftriaxone					X		■	X	X	X
Cefotaxime					X		X	■		X
Cefepime							X		■	
Ceftazidime							X	X		■

Common continuous infusion β-lactams
- Penicillin
- Oxacillin
- Cefazolin
- Piperacillin/tazobactam

Ceftriaxone dosing in adults
- 1gm daily (most infections)
- 2gm daily (some infections)
- 2gm BID (endocarditis & meningitis)

No renal dose adjustments
- Oxacillin
- Nafcillin
- Ceftriaxone

Abbreviations: AUC = area under the curve, BLI = β-lactamase inhibitor, Cmax = maximum concentration, DOC = drug of choice, ESBL = extended spectrum β-lactamase, IV = intravenous, MDR = multi drug-resistant, MIC = minimum inhibitory concentration, MSSA = methicillin-sensitive *Staphylococcus aureus*, MRSA = methicillin-resistant *Staphylococcus aureus*, PCN = penicillin

Beta-Lactam/Beta-Lactamase Inhibitor Cheat Sheet

β-lactams interfere with the bacterial cell wall by interacting with penicillin binding proteins. β-lactamases are enzymes which hydrolyze the β-lactam ring and render β-lactams inactive. β-lactamase inhibitors neutralize β-lactamases and allow their β-lactam counterpart to work.

- β-lactamase inhibitors can overcome β-lactamase enzymes but won't impact drug resistance from other mechanisms (*e.g.*, efflux pumps, porin channels)
- Amoxicillin-clavulanic acid and ampicillin-sulbactam have a very similar spectrum of antibacterial activity
  - Both are go-to agents for bite wounds caused by humans or animals
- Piperacillin-tazobactam has better *E. coli* coverage than amoxicillin-clavulanic acid or ampicillin-sulbactam, but all three have good anaerobic activity
- Ceftolozane-tazobactam and ceftazidime-avibactam do not have good anaerobic activity, combine with metronidazole for intra-abdominal infection treatment
- The main role for newer BL/BLIs has been in treating carbapenem-resistant Gram negative bacteria
  - None of the new BL/BLIs are available as a generic product and all are expensive
  - The new BL/BLIs have helped serve as an alternative to nephrotoxic Gram negative drugs like the aminoglycosides and polymyxins (*e.g.*, colistin)

Generic	Brand	FDA Approval	Route	Usual Adult Dose Range	Renal Adjust Doses	Infusion Time	Pseudomonas Activity	MRSA Activity	Notes
Amoxicillin-clavulanic acid	Augmentin®	1996	PO	Varies by product	Yes	-	No	No	Is available IV in some countries outside the United States
Ampicillin-sulbactam	Unasyn®	1997	IV	1.5 – 3 gm every 6-8 hrs	Yes	30 mins	No	No	Sulbactam alone can have Acinetobacter activity
Piperacillin-tazobactam	Zosyn®	2005	IV	3.375 – 4.5 gm every 6-8 hrs	Yes	30 mins*	Yes	No	One of the most over-used IV antibiotics in hospitals
Ceftolozane-tazobactam	Zerbaxa®	2014	IV	1.5 – 3 gm every 8 hrs	Yes	1 hr	Yes	No	Can kill carbapenem-resistant Pseudomonas
Ceftazidime-avibactam	Avycaz®	2015	IV	2.5 gm every 8 hrs	Yes	2 hrs	Yes	No	Can kill carbapenem-resistant Enterobacterales
Meropenem-vaborbactam	Vabomere®	2017	IV	4 gm every 8-12 hrs	Yes	3 hrs	Yes	No	Can kill carbapenem-resistant Enterobacterales
Imipenem-relebactam	Recarbrio®	2019	IV	1.25 gm every 6 hrs	Yes	30 mins	Yes	No	Can kill imipenem-resistant *Pseudomonas-aeruginosa*

*Piperacillin-tazobactam is commonly given over 3 or 4 hours in hospitals as part of extended-infusion protocols which prolong time above the MIC (*i.e.*, increase bacterial killing)
-Note: Enterobacterales (formerly called Enterobacteriaceae) include *E. coli* and *K. pneumoniae*, but do not include *Pseudomonas aeruginosa* or *Acinetobacter baumannii*

- The Ambler Classification has been used to differentiate types of β-lactamases and BLIs have various capacity to work against them, in general…
  - Can have Ambler class A activity (*e.g.*, KPC): avibactam, tazobactam (less), vaborbactam, relebactam
  - Can have Ambler class B activity (*e.g.*, NDM, IMP, VIM): none
  - Can have Ambler class C activity (*e.g.*, AmpC): avibactam, tazobactam (less), vaborbactam, relebactam
  - Can have Ambler class D activity (*e.g.*, OXA): avibactam
  - Combining aztreonam with avibactam or vaborbactam has been shown to have activity versus NDM and OXA β-lactamase producing GNRs

Abbreviations: BL = beta-lactam, BLI = beta-lactamase inhibitor, GNR = Gram negative rod, IMP = imipenemase, IV = intravenous, KPC = Klebsiella pneumoniae carbapenemase, NDM = New Delhi metallo-β-lactamase, OXA = oxacillinase, PO = oral, VIM = Verona integron-encoded metallo-β-lactamase

Glycopeptides Cheat Sheet

	Vancomyicn	Daptomycin (Cubicin)	Telavancin (Vibativ)	Oritavancin (Orbactiv, Kimyrsa)	Dalbavancin (Dalvance)
FDA Approval	A long time ago	2003	2009	2014[Orbactiv], 2021[Kimyrsa]	2014
Available generic	Yes	Yes	No	No	No
Mechanism of action	Inhibits d-ala, d-ala, interfering w/ the cell wall	Bacterial cell wall depolarizer	Inhibits d-ala, d-ala + cell wall depolarizer	Inhibits d-ala, d-ala and binds to stem peptides interfering w/ the cell wall	Inhibits d-ala, d-ala, interfering w/ the cell wall
Half-life	Hours	Hours	Hours	Days	Days
General adult dosing	15 mg/kg Q12h (IV) // 125mg Q6h (PO)	6-10 mg/kg IV Q24h	10mg/kg IV Q24h	1.2gm IV once	1.5 gm IV once **or** 1 gm IV followed by 500 mg IV a week later
Streptococci	+	+	+	+	+
MRSA	+	+	+	+	+
Enterococci	+	+	+	+	+
VRE	-	+	+/-	+	+/-
Clostridioides difficile	GI route only	-	-	-	-
Gram-negative bacilli	-	-	-	-	-
Monitor levels	Yes	No	No	No	No
Renal adjust (CrCl)	Yes, depends	< 30	< 50	Maybe < 30	< 30
Infusion time	≥ 60 min/gram	2 minutes (adults only)	1 hour	3 hours for Orbactiv, 1 hour for Kimyrsa	0.5 hours

Daptomycin Dosing Highlights

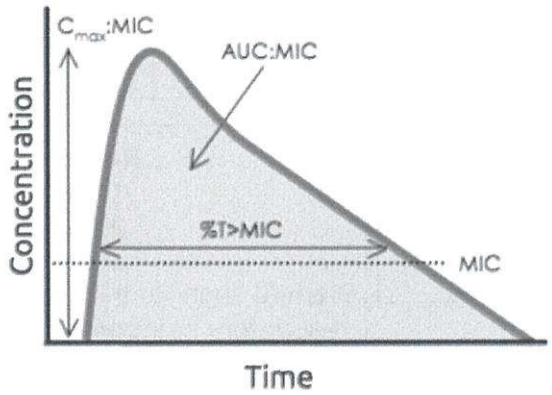
- Not for pneumonia, inactivated by lung surfactant
- Can cause CK elevation, beware rhabdomyolysis
- Does not cause histamine-mediated infusion reactions
- A go-to drug for VRE bloodstream infections

Vancomycin Dosing Highlights

- Usually dosed using actual body weight
- Measure levels to balance efficacy vs toxicity
  - Common initial trough goal is 15-20 mcg/mL
  - Troughs above 25 associated with nephrotoxicity
- Loading dose usually indicated for critically ill patients
- Renal function tied directly to vancomycin clearance

Vancomycin Infusion Reaction

- Not an allergic reaction. Upper body flushing, urticaria, pruritis, and/or rash. Caused by histamine release when infused too quickly. Many times can be resolved with use of anti-histamines and slower infusion rates. Infusion is usually at least one hour per gram of vancomycin.



- Glycopeptide mechanisms vary depending on the bug-drug combination and can be time-dependent, AUC:MIC dependent, or concentration-dependent.
- Of particular importance for vancomycin versus MRSA an AUC:MIC > 400 is desired, but if the MRSA MIC to vancomycin is >1 this may not be enough and alternative drugs should be considered.

Miscellaneous Notes...

- Daptomycin, telavancin, oritavancin, and dalbavancin are actually lipoglycopeptides
- Vancomycin is widely considered the DOC for *Corynebacterium* (IV) and *C. difficile* (PO)
- There is a Cubicin RF formulation, which is allows better stability and storage of daptomycin
- Vancomycin resistance is conferred via Van genes (*e.g.*, VanA, VanC), which cause a change in the binding site from d-ala, d-ala to d-ala, d-lac. Van genes can confer resistance to other glycopeptides
- Thickening bacterial cell walls may increase resistance in MRSA to vancomycin and daptomycin, beware MIC > 1
- Telavancin is not commonly used in clinical practice, while vancomycin is very frequently over-used in hospitals
- Oritavancin and dalbavancin are being used in emergency departments and outpatient to prevent hospitalizations
- Vancomycin oral has poor systemic absorption and is only to be used for *C. difficile* infection

Abbreviations: AUC = area under the curve, Cmax = maximum concentration, DOC = drug of choice; MIC = minimum inhibitory concentration, MRSA = methicillin-resistant *Staphylococcus aureus*, VRE = vancomycin-resistant Enterococci

Fluoroquinolones Cheat Sheet

Mechanisms of Action

1. Targets DNA gyrase (topoisomerase II), causing excess supercoiling that arrests DNA replication
2. Targets topoisomerase IV, interfering with separation of daughter DNA molecules

Target affinity: Fluoroquinolones have different affinity for these targets. For example ciprofloxacin has more DNA gyrase activity, making it more targeted towards Gram negative organisms.

Killing: Generally considered to have concentration-dependent (*e.g.*, AUC:MIC) bactericidal activity, however pharmacodynamics can vary from organism to organism

Fluoroquinolone Comparison

	Ciprofloxacin	Levofloxacin	Moxifloxacin	Delafloxacin
Brand name	Cipro	Levaquin	Avelox	Baxdela
FDA approval	1994	1996	1999	2017
Available IV	Yes	Yes	Yes	Yes
Available PO	Yes	Yes	Yes	Yes
Oral bioavailability	80%	100%	> 90%	67%
Typical adult dose	500 mg PO BID 400 mg IV BID	250-750 mg PO or IV daily	400 mg PO or IV daily	450 mg PO BID or 300 mg IV BID
Adjust doses for renal function	CrCl < 50 for PO CrCl < 30 for IV	CrCl < 50	No	eGFR < 30
Streptococcus pneumoniae	+/-	+++	+++	+++
Pseudomonas aeruginosa	+++	++	-	+++
Anaerobes	-	-	++	++
Atypicals	+++	+++	+++	+++

Resistance Genes
GyrA
GyrB
ParC

Respiratory FQs
1. Levofloxacin
2. Moxifloxacin
3. Gemifloxacin

Named such for their activity versus the common respiratory pathogen *Streptococcus pneumoniae*

FDA Boxed Warnings
1. Tendonitis
2. Tendon rupture
3. CNS effects
4. Peripheral neuropathy
5. Worsening of myasthenia gravis

Other Possible Side Effects
- Qt interval prolongation
- Photosensitivity
- Hypoglycemia (including coma)
- Altered mental health
- Diarrhea
- Aortic dissection

- The base molecule for all FQs is nalidixic acid
- Beware *E. coli* resistance to FQs
- FQ use is linked to MRSA infection and FQ resistance in GNRs
- FQs are a high-risk drug classes for causing *C. difficile* infection
- Beware drug-drug interaction between FQs and warfarin
- FQs have a variety of ophthalmic and otic preparations
- FQs can offer oral formulations that cover *Pseudomonas* sp.
- Per the FDA, FQs are not 1st line drugs for acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis, or uncomplicated UTI
- Generally avoid FQ monotherapy for Enterococci and Staphylococci, although delafloxacin may be an exception by having a role as monotherapy versus MRSA
- In general avoid moxifloxacin for UTI due to low urine concentrations compared to other FQs
- FQs are widely considered the DOC for prostatitis due to excellent penetration into the prostate
- FQs can have a role for treating *Mycobacterium tuberculosis* and non-tuberculosis mycobacterium
- FQs bind to cations (*e.g.*, calcium, magnesium, aluminum) when given orally at the same time, which means they may need to be separated from meals or other drugs

Abbreviations: ABX = antibiotics, DOC = drug of choice, FQ = fluoroquinolone, GNRs = gram negative rods, UTI = urinary tract infection

Tetracycline Cheat Sheet

Mechanism of Action

Tetracycline antibiotics work by inhibiting the 30S ribosomal subunit of susceptible bacteria, which interferes with bacterial protein synthesis.
→ Tetracyclines are primarily bacteriostatic, but there are scenarios in which they can exhibit bactericidal activity.
→ Newer tetracyclines can have a greater spectrum of activity due to less efflux-mediated resistance and tighter binding at their site of action.

Comparison of Tetracycline Antibiotics

	Doxycycline	Minocycline	Tigecycline	Eravacycline	Omadacycline
Brand name	Doryx, Vibramycin	Minocin, Solodyn	Tygacil	Xerava	Nuzyra
FDA-approval	1967	1971	2009	2018	2018
Typical adult dose	100mg Q12H	200mg x1, then 100mg Q12H	100mg x1 loading dose, then 50mg Q12H	1mg/kg IV Q12H	Per indication. IV and PO differ. Requires loading dose.
Formulations	IV, PO	IV, PO	IV	IV	IV, PO
Renal adjust	No	No	No	No	No
Hepatic adjust	No	No	Child Pugh C	Child Pugh C	No
MRSA activity	Yes	Yes	Yes	Yes	Yes
VRE activity	No	No	Yes	Yes	Yes
Anaerobic activity	Fair	Fair	Good	Good	Good
Gram negative activity	Fair	Fair	Good	Good	Good
Side effects	Esophagitis, photosensitivity	Esophagitis, photosensitivity	Nausea[$], vomiting[$], HA, pancreatitis, hepatic effects	Nausea, vomiting, infusion site reactions	Nausea, vomiting, HA, hepatic effects, infusion site reactions
Other	DOC for Lyme disease. Used for MRSA skin infections, acne, and rosacea	Has activity versus *Stenotrophomonas.* Used for acne.	Poor serum concentrations. Has a FDA boxed warning for increased death.	FDA-approved for cIAI in adults.	FDA-approved for CABP and ABSSSI. Carries warning for mortality imbalance w/ CABP.
Class effect	Tooth discoloration, enamel hypoplasia, bone growth inhibition → generally avoid use in < 8 years of age. This is a debated topic.				

Tetracycline is not included because numerous supply issues and infrequent use in clinical practice reduce the current clinical relevance (except for *H. pylori*).
[$]Nausea and vomiting with tigecycline can be particularly problematic. Eravacycline and omadacycline (IV > PO) may have less nausea and vomiting.

HIGHLIGHTS

- Notable tetracycline resistance is conferred by the "tet" genes (*e.g.*, tetA, tetM). This resistance is typically related to increased efflux or ribosomal protection
- Tigecycline's major hole in coverage is *Pseudomonas aeruginosa.* Eravacycline and omadacycline also lack coverage for *Pseudomonas.*
- Doxycycline hyclate and doxycycline monohydrate are equally clinically effective. They are just different salt forms of doxycycline.
- Periostat (doxycycline 20mg tablets taken Q12H) is only indicated for periodontitis. Oracea (doxycycline 40mg tablet taken Q24H) is only indicated for rosacea
  -Anti-inflammatory effects of doxycycline have garnered interest amongst dermatologists and contributed to the development of Oracea
- Tetracyclines (similar to fluoroquinolones and macrolides) have activity versus many atypical bacteria (*e.g.*, *Legionella*, *Mycoplasma*, *Chlamydia*)
- Tetracyclines have many uses, including for malaria prophylaxis, mycobacterium infection, VRE cIAI, community-acquired MRSA skin infection, and acne
- The utility of the newer tetracyclines eravacycline and omadacycline is likely to be for infections due to multi-drug resistant bacteria

Abbreviations: ABSSSI = acute bacterial skin & skin structure infections, CABP = community-acquired bacterial pneumonia, cIAI = complicated intra-abdominal infection, CrCl = creatinine clearance, DOC = drug of choice, ESBL = extended-spectrum β-lactamase, HA = headache, VRE = vancomycin-resistant Enterococci

Macrolides & Clindamycin Cheat Sheet

Mechanisms of Action

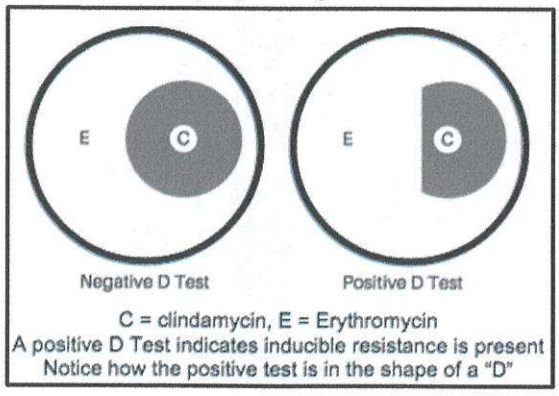
Macrolides and clindamycin are not chemically related, but both bind to the 50S ribosomal subunit of susceptible bacteria, thus interfering with protein synthesis in susceptible bacteria
→ Clindamycin and macrolides can be bacteriostatic or bactericidal depending on the bacteria and drug concentration at the site of infection
→ The *erm* genes have been associated with macrolide and clindamycin resistance

Comparison of Macrolides[1] & Clindamycin

	Erythromycin	Clarithromycin	Azithromycin	Clindamycin
Select brand name	Ery-Tab	Biaxin, Biaxin XL	Zpak, Zithromax, Zmax	Cleocin
Class	Macrolide	Macrolide	Macrolide	Lincosamide
FDA-approval	1983	1991	1994	1970
Generic available	Yes	Yes	Yes	Yes
Systemic formulations	IV, PO	PO	IV, PO	IV, PO
Typical PO adult dose	Varies by formulation[2]	250-500 mg Q12H, XL is 1 gm Q24h	250-500 mg Q24H	150-900 mg given Q6H, Q8H, or Q12H
Half-life	2 hours	6 hours	68 hours	4 hours
Renal adjust	No	CrCl < 30	No	No
Hepatic adjust	No	No	No	No
Pregnancy category	B	C	B	B
Side effects	GI effects, QTc prolongation	GI effects, QTc prolongation	GI effects (less), QTc prolongation	Diarrhea, including *C. difficile* infection
Other	A motilin-agonist, used for GI motility	An important drug for NTM infections	NOT first-line for acute bronchitis, sinusitis, or pharyngitis	A common drug use in penicillin-allergic patients

[1]Fidaxomicin (Dificid) is a macrolide, but has been excluded since it is exclusively used for *C. difficile* infection
[2]400mg erythromycin ethylsuccinate produces the same serum concentrations as 250mg erythromycin stearate or base

- Clindamycin has anti-toxin effects, which can help treat necrotizing infections due to Streptococci or Staphylococci
- Clindamycin has good anaerobic activity, but is not reliable for *Bacteroides fragilis* and lacks *Clostridioides difficile* activity
- Beware clindamycin resistance in MRSA, especially with hospital-acquired MRSA. A D-test is used to confirm susceptibility, which can detect the *erm* gene (an inducible type of resistance other tests may not identify) – see D-test image >>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>>
- Clindamycin can be combined with pyrimethamine to treat encephalitis or pneumonitis caused by *Toxoplasma gondii*
- Macrolides are commonly considered for infection due to atypical organisms (*e.g.*, Chlamydia, Mycoplasma, Legionella)



C = clindamycin, E = Erythromycin
A positive D Test indicates inducible resistance is present
Notice how the positive test is in the shape of a "D"

- Azithromycin 1gm x1 is second line for chlamydia in adults, after doxycycline 100mg BID x7 days
- Azithromycin comes as a "Z-Pak" dosed 500mg x1 on day 1, then 250mg daily x4 days
- Beware that while a Z-Pak may be prescribed for CAP, *Streptococcus pneumonia* resistance rates can be a problem
- For CD4 < 50, azithromycin 1200mg weekly is preferred for primary prophylaxis vs *Mycobacterium avium Complex*
- Azithromycin generally has less side effects and less drug-drug interactions than clarithromycin or erythromycin so in turn azithromycin is used more frequently in clinical practice
- Erythromycin topical is commonly used for prophylaxis in newborns to prevent gonococcal ophthalmia neonatorum
- Macrolides play an important role in the treatment of *H. pylori*, which requires combination therapy for treatment
- Macrolides are sometimes employed for their anti-inflammatory effects and to help prevent pulmonary exacerbation
- Some studies have found macrolides are associated with increases in cardiac events, however this is still debated

Abbreviations: CAP = community acquired pneumonia, CrCl = creatinine clearance, HIV = human immunodeficiency virus, IV = intravenous, MRSA = methicillin-resistant *Staphylococcus aureus*, NTM = non-Tuberculosis mycobacterium, PO = oral

Pneumonia Cheat Sheet

Pneumonia Definitions

Community acquired pneumonia (CAP): an acute pulmonary parenchyma infection acquired in the community
Hospital acquired pneumonia (HAP): occurs ≥48 hours after hospital admission, not incubating at admission
Ventilator-associated pneumonia (VAP): HAP + develops ≥48 hours after endotracheal intubation
Note: The term healthcare-associated pneumonia (HCAP) had been used to identify patients at risk for infection with drug-resistant organisms, but was found to be overly sensitive and was dropped from IDSA guidelines.

- CAP organisms: *Streptococcus pneumoniae* (most common), *Haemophilus influenzae*, *Moraxella catarrhalis*, atypical bacteria (e.g., *Mycoplasma pneumoniae*, *Legionella pneumophilia*, *Chlamydia pneumoniae*)
  - *Strep. pneumoniae* is alpha-hemolytic Gram positive cocci in pairs or chains
- HAP & VAP organisms: above plus MRSA, *Pseudomonas aeruginosa,* and other Gram negative rods
- For pneumonia related to aspiration, routinely covering anaerobes is only required if abscess/empyema is suspected
- Use local resistance / epidemiological data + patient-specific data to identify potential pathogens/ resistance
- There are many strong and weak risk factors for infection or colonization with MRSA or *Pseudomonas*

Comparison of Select Oral Drugs Used For Pneumonia

	Azithromycin	Amoxicillin/ clavulanic acid	Cefuroxime axetil	Doxycycline	Levofloxacin/ Moxifloxacin
Brand name	Zithromax, Zpak	Augmentin	Ceftin	Vibramycin, Doryx	Levaquin, Avelox
Mechanism	Interferes with protein synthesis, inhibits 50S ribosomal subunit	Binds to penicillin binding proteins, inhibiting cell wall synthesis	Binds to penicillin binding proteins, inhibiting cell wall synthesis	Interferes with protein synthesis, inhibits 30S ribosomal subunit	Inhibit DNA gyrase + topoisomerase
ılf-life	3 days	1 hour	1 hour	1 day	L: 6-8 hours M: 12 hours
Typical adult dose	500 mg x1, then 250 mg daily	500-875 mg BID	500 mg BID	100 mg BID	L: 500-750 mg daily M: 400 mg daily
Atypical activity	Yes	No	No	Yes	Yes
Renal adjust	No	CrCl < 30	CrCl < 30	No	L: CrCl < 50; M: No
Side effects	QT prolongation, GI effects	Diarrhea, hypersensitivity	Diarrhea, hypersensitivity	Esophagitis, photosensitivity	Many. See below + QT prolongation, photosensitivity, hypoglycemia
Notes	Beware *Strep. pneumoniae* resistance	Reserve use for known susceptibility	Cefpodoxime is an oral 3rd-gen ceph option	Avoid in children < 8 years b/c tooth and tissue ADRs	Reserve use when possible b/c ADRs

Drugs with *Pseudomonas aeruginosa* Activity

- Amikacin
- Aztreonam
- Ceftazidime
- Ceftazidime-avibactam
- Ceftolozane-tazobactam
- Cefepime
- Ciprofloxacin
- Colistin (polymyxin E)
- Delafloxacin
- Doripenem
- Gentamicin
- Imipenem-cilastatin
- Imipenem-cilastatin-relebactam
- Levofloxacin
- Meropenem
- Meropenem-vaborbactam
- Piperacillin-tazobactam
- Plazomicin
- Polymyxin B
- Tobramycin

Fluoroquinolone FDA Boxed Warnings

1. Tendonitis
2. Tendon Rupture
3. CNS effects
4. Peripheral neuropathy
5. Worsening of myasthenia gravis

- Macrolides, fluoroquinolones, and tetracyclines are go-to drugs for atypical organisms
- Moxifloxacin & levofloxacin are "respiratory fluoroquinolones" for their coverage of *Strep. pneumo*
- Ceftriaxone + azithromycin = common inpatient CAP regimen
- If MRSA coverage is needed, use either linezolid or vancomycin. Doxycycline may also be an option.
  Daptomycin should never be used for pneumonia, since it is inactivated by lung surfactant
  For suspected HAP, a negative MRSA colonization status has a high negative predictive value for MRSA pneumonia, and therefore can be used to help discontinue empiric anti-MRSA therapy

Abbreviations: ADR = adverse drug reactions, CAP = community acquired pneumonia, MRSA = methicillin-resistant *Staph. aureus*

Urinary Tract Infection Cheat Sheet

Bacteriuria (bacteria in the urine) Definitions

- In women = 2 consecutive voided urine samples with the same bacteria at a quantity $\geq 10^5$ CFU/mL
- In men = a single, clean catch voided urine sample with 1 bacteria at a quantity $\geq 10^5$ CFU/mL
- In catheterized patients = a catheterized urine sample with 1 bacteria at a quantity $\geq 10^2$ CFU/mL
- Pyuria (WBCs in urine) alone + ASB is **not** an indication for antibiotic treatment
- ASB rarely requires treatment, but exceptions can be: pregnancy, recent transplant, upcoming urological procedure that includes mucosal bleeding

- Possible UTI s/sx: dysuria, frequency, urgency, abdominal pain. With systemic symptoms of fever, flank pain or costovertebral angle (CVA) tenderness, beware pyelonephritis (aka kidney infection aka upper UTI)
- Cloudy, foul smelling urine alone is a poor indicator of UTI, more information is needed to make a UTI diagnosis
- After *Escherichia coli*, another important UTI pathogen to beware is *Staphylococcus saprophyticus*
- Beware yeast or Enterococci in the urine may be contaminant given proximity of the GU tract to the GI tract

Comparison of Select Oral UTI Drugs

	Sulfamethoxazole /trimethoprim	Nitrofurantoin	Ciprofloxacin	Amoxicillin/ clavulanic acid	Fosfomycin
Brand name	Bactrim, Septra	Macrobid, Macrodantin	Cipro, Cipro XR	Augmentin	Monurol
Mechanism	Folate synthesis inhibitor	Inhibit bacterial protein synthesis	Inhibit DNA gyrase + topoisomerase	Binds to penicillin binding proteins, inhibiting cell wall synthesis	Inhibits pyruvyl transferase, inhibiting cell wall synthesis
Typical adult dose for UTI	1 DS tablet BID	100mg BID (Macrobid) 50-100mg Q6H (Macrodantin)	250-500mg BID (cipro) 500-1000mg Q24H (Cipro XR)	500-875mg BID	3gm PO for cystitis in a woman
Renal adjust	CrCl < 30	Avoid CrCl < 30	CrCl < 50	CrCl < 30	No
E. coli resistance	25-35%	5-10%	25-35%	High	5%
OK for upper UTI	Yes	No	Yes	Yes**	No
Side effects	Rash, hyper-K+	Pulmonary toxicity (repeated or long-term use)	Many. See below + QT prolongation, photosensitivity	Diarrhea, hypersensitivity	Diarrhea, but well tolerated
Notes	Beware sulfa allergy	A good empiric drug	Generally avoid FQs when possible	Reserve use for culture-directed tx	Expensive, use for MDROs

Oral cephalosporins not included due to lack of space; Typically beta-lactams require a longer duration of therapy

Methenamine (Hiprex)

- ✓ Prophylaxis only
- ✓ Need urine pH $\leq$ 5.5
- ✓ Converts to formaldehyde
- ✓ No resistance concern
- ✓ Not for chronic cath patients
- ✓ Avoid w/ sulfas or gout

When to Avoid Nitrofurantoin

- ✓ Known resistant organism
- ✓ CrCl < 30 or very elderly
- ✓ Concern for prostatitis
- ✓ Upper UTI or systemic infection
- ✓ For long-term/ repeated courses

Fluoroquinolone Boxed Warnings

1. CNS effects
2. Tendonitis
3. Tendon rupture
4. Peripheral neuropathy
5. Worsen existing myasthenia gravis

- 1st questions for a positive urine cx: (1) why/how was it collected?, (2) is it a contaminant?, (3) any symptoms?
- Nearly all chronically catheterized patients will have a positive urine culture, but do not need antibiotics
- Generally avoid for UTI due to low urine concentrations: moxifloxacin, tigecycline, micafungin, polymyxin B
- Fluoroquinolones remain a go-to drug class for prostatitis (usually ciprofloxacin or levofloxacin)
- In a male UTI is considered "complicated", but nitrofurantoin may still be an option for lower UTI in a male
- Beware drug-drug interactions with any UTI drugs and warfarin

Abbreviations: ASB = asymptomatic bacteriuria, cx = culture, FQ = fluoroquinolone, MDR = multidrug resistant organisms, s/sx = signs and symptoms, SMX/TMP = sulfamethoxazole/ trimethoprim, tx = treatment, UTI = urinary tract infection

Malaria Cheat Sheet

The CDC weblage "Malaria for Travelers for U.S. Residents" is an essential page on malaria.
Find it at: https://www.cdc.gov/malaria/travelers/index.html

- Malaria in humans is a disease caused by a protozoa parasitic organisms of the *Plasmodium* genus
- The vector of *Plasmodium* spp. is the female mosquitoes of the *Anopheles* species (the males don't bite)
  - Is not the same vector as for dengue, yellow fever, chikungunya, or Zika (*Aedes* sp. mosquitos spread these)
- *Plasmodium falciparum* and *Plasmodium vivax* are the two most common species, but other notable species are *Plasmodium ovale, Plasmodium malariae*, and *Plasmodium knowlesi*
- The types of *Plasmodium* species and drug resistance which they carry varies geographically worldwide, which is why the website noted above is important for travelers who may need pre-exposure prophylaxis or treatment
- Some say "fever in a traveler is malaria until proven otherwise" because malaria is the most common cause of acute fever in travelers to sub-saharan Africa and some tropical regions
- Blood smears and parasite density are used in the diagnosis of malaria with 1% density as a key cut-off value
- Need malaria treatment or prophylaxis? → Consider: Plasmodium species, resistance, and severity of illness
- *P. vivax* and *P. ovale* have dormant forms called hypnozoites, which can emerge from the liver years after infection, which can cause relapse if not treated adequately
- The CDC's Yellow Book on health information for international travel is a resource worth knowing about

Generic	Brand	Route	Px	Tx	Frequency	Notes
rtesunate	-	IV	-	✓	BID x3 doses, then daily PRN	• Used to treat severe malaria • Continuation depends on parasite density >1% • Available through CDC or commercially • Has a warning for post-treatment hemolysis
Atovaquone-lumefantrine	Coartem	PO	-	✓	Initial dose, 8h later, then BID	• Approved for acute, uncomplicated malaria due to *Plasmodium falciparum*, for which it is first-line per CDC • Beware QTc prolongation, hypo-K^+ and hypo-Mg^{++}
Atovaquone-proguanil	Malarone	PO	✓	✓	Daily	• Can start w/in 1-2 days of travel, good for last minute travel • Use contraindicated with creatinine clearance < 30 mL/min • Less affordable
Chloroquine	Aralen	PO	✓	✓	Weekly	• Cannot use in areas of chloroquine or mefloquine resistance • May exacerbate psoriasis • Can be used in all trimesters of pregnacy
Mefloquine	Lariam	PO	✓	✓	Weekly	• Avoid if hx of seizures or certain psychological disorders • Can be used during pregnancy
Primaquine	-	PO	✓	✓	Daily	• Excellent for *Plasmodium vivax* px • Cannot use if patient has G6PD defficiency (must test) • Cannot be used by pregnant women
Tafenoquine	Arakoda, Krintafel	PO	✓	-	Daily	• Cannot use if patient has G6PD defficiency (must test) • Excellent for *Plasmodium vivax* px and also has activity versus *Plasmodium falciparum* • Cannot be used by pregnant women or children • Not recommended for use with psychological disorder • Can be used as anti-relapse treatment
Doxycycline	Vibramycin	PO, IV	✓	✓	Daily	• Can start w/in 1-2 days of travel, good for last minute travel • More affordable

Tetracycline, clindamycin, hydroxychloroquine (Plaquenil), and quinine are other drugs used for Malaria

Abbreviations: CDC = Center for Disease Control & Prevention, hx = history, IV = intravenous, K = potassium, Mg = magnesium, px = prophylaxis, PO = oral, tx = treatment

Antimicrobial Toxicities Rapid Fire Test

Question #1
What antibiotic that colors secretions red/orange is associated with hepatotoxicity?

Question #2
What are the 5 FDA black box warnings on fluoroquinolone antibiotics?

Question #3
What common toxicity do vancomycin, aminoglycosides, and amphotericin B all share?

Question #4
What is a major side effect of clindamycin that commonly impacts clinical decision making?

Question #5
What shared cardiac toxicity do macrolides, fluoroquinolones, telavancin, and azole antifungals share?

Question #6
What side effect is associated with high doses of beta-lactams and particularly with the carbapenem imipenem-cilastatin?

Question #7
All beta-lactam antibiotics can cause this side effect, but it was the reason methicillin was removed from the market in the US. What side effect is it?

Question #8
Oral bisphosphonates can cause significant esophagitis. What class of antibiotics also can cause significant esophagitis, when given orally?

Question #9
What intravenous drug that has Gram positive activity only has a potential side effect of eosinophilic pneumonia?

Question #10
What class of intravenous antibiotics used mostly for Gram negative bacteria is associated with ototoxicity?

Question #11
What electrolyte abnormality is associated with sulfamethoxazole-trimethoprim (SMX-TMP, Bactrim, Septra), especially at higher doses?

Question #12
What two electrolyte abnormalities are associated with the antifungal drug amphotericin B?

Question #13
What type of toxicity is long-term or repeated use of nitrofurantoin associated with?

Question #14
What type of toxicity is long-term or repeated use of metronidazole associated with?

Question #15
What type of oral toxicity is metronidazole associated with?

Question #16
What side effect is associated with the use of ceftriaxone in premature infants?

Question #17
When administered too quickly, what reaction can vancomycin, oritavancin, dalbavancin, or telavancin cause?

Question #18
What side effect does erythromycin cause so frequently it is rarely used orally for infections?

Question #19
What are the two most important side effects to know about colistin (colistimethate, polymyxin E)?

Question #20
What requires close attention on the CBC when employing linezolid or tedizolid?

Question #21
What two toxicities are associated with linezolid and tedizolid use for greater than 28 days?

Question #22
What medication used for treating Mycobacterium tuberculosis is associated with toxicity of the eye?

Question #23
What medication used for treating Mycobacterium tuberculosis is combined with pyridoxine (vitamin B-6) to prevent peripheral neuropathy?

Question #24
What common concerning adverse effect do the antiviral drugs foscarnet and cidofovir share?

Question #25
What side effect is anti-CMV drug ganciclovir associated with, which causes the need for lab monitoring?

Question #26
What is a side effect that can occur with high-dose IV acyclovir and is a reason to give NS blouses during such therapy?

Question #27
What side effect is associated with voriconazole when levels exceed 5.5?

Question #28
What is a major potential toxicity associated with ketoconazole, which is the reason it is not commonly used orally?

Question #29
What is the adverse reaction that has earned amphotericin B the nickname "amphoterrible"?

Question #30
What is one major side effect associated with quinupristin/dalfopristin (Synercid)?

ANSWERS

Question #1 answer: Rifampin

Question #2 answer: 1. Peripheral neuropathy 2. Tendonitis 3. Tendon rupture 4. CNS effects 5. Can worsen myasthenia gravis

Question #3 answer: Nephrotoxicity

Question #4 answer: Diarrhea

Question #5 answer: QT prolongation

Question #6 answer: Seizures

Question #7 answer: Interstitial nephritis

Question #8 answer: Tetracyclines

Question #9 answer: Daptomycin

Question #10 answer: Aminoglycosides

Question #11 answer: Hyperkalemia

Question #12 answer: 1. Hypokalemia 2. Hypomagnesemia

Question #13 answer: Pulmonary toxicity (e.g., pulmonary fibrosis)

Question #14 answer: Peripheral neuropathy

Question #15 answer: Metallic taste

Question #16 answer: Sludging of the gallbladder

Question #17 answer: Vancomycin infusion reaction (note this is a histamine-mediated reaction and not an allergy) and also that oritavancin product Kimyrsa is infused as 1200 mg over 1 hour while Orbactiv is infused as 1200 mg over 3 hours.

Question #18 answer: Diarrhea (erythromycin is a motilin agonist and has more GI side effects as compared to clarithromycin or azithromycin. Sometimes for this reason it is used for GI motility)

Question #19 answer: 1. Nephrotoxicity 2. Neurological toxicity

Question #20 answer: Platelets (beware thrombocytopenia), which seems to be more common with >7-14 days of therapy

Question #21 answer: 1. Optic neuritis (potentially blindness) 2. Peripheral neuropathy

Question #22 answer: Ethambutol

Question #23 answer: Isoniazid

Question #24 answer: Nephrotoxicity

Question #25 answer: Myelosuppression

stion #26 answer: Crystaluria

Question #27 answer: 1. Changes in color perception (blues and greens) 2. Auditory and visual hallucinations

Question #28 answer: Hepatotoxicity

Question #29 answer: Infusion mediated reactions (e.g., fever, hypotension, chills, rigors)

Question #30 answer: Hyperbilirubinemia Thrombophlebitis (it "blows lines") Arthralgias / myalgias

Antifungals Memorization Sheet

Fungi can be categorized as _____, _____, or _____

_____and _____are yeasts

Important Candida species include *Candida* _____, *Candida* _____, *Candida* _____, *Candida* _____, and *Candida* _____

Candida _____ is an emerging fungal pathogen and is commonly _____ to at least one class of antifungal drugs

_____, _____, _____, _____, and _____ are moulds and zygomycetes

_____, and _____, are moulds but not zygomycetes

_____, _____, _____, and _____ are dimorphic fungi

Name the generic name for each of the following brand names:

Diflucan = _____ Sporanox = _____ VFEND = _____ Noxafil = _____

Cresemba = _____ Mycamine = _____ Eraxis = _____ Cancidas = _____

Abelcet = _____ Fungizone = _____ Ambisome = _____

Azoles work by interfering with _____ synthesis, which is the principal _____ in the fungal _____

_____ (and many other azoles) is _____ versus most yeasts (*e.g.*, Candida species) and _____ versus many moulds

Candida _____ can be susceptible dose-dependent (SDD) tor resistant to fluconazole

Candida _____ is intrinsically resistant to fluconazole

_____ is generally considered the drug of choice for treating Aspergillus species

Echinocandins work by _____, a component of the fungal _____

Echinocandins exhibit _____ activity versus many Candida species

Polyenes work by binding to _____ and altering fungal _____ leading to leakage of cell components and fungal cell death

Polyenes are generally _____ antifungals

Most azoles have excellent _____ and are good candidates for IV to PO programs. Echinocandins are only available _____.

Azole antifungals are notorious for drug-drug interactions as _____ or _____ of CYP-450, beware elevation of _____ from azoles

Polyene toxicities of utmost importance include _____, _____, _____, and _____

Conventional amphotericin B is associated with more _____ than amphotericin B lipid or liposomal

Therapeutic drug monitoring is commonly employed for _____ (typical goal range _____) and _____ (typical goal range _____)

ANSWERS

Fungi can be categorized as _*yeasts*_, _*moulds*_, or _*dimorphic fungi*_

_*Candida*_and _*Cryptococci*_are yeasts

Important Candida species include *Candida _albicans_*, *Candida _glabrata_*, *Candida _krusei_*, *Candida _auris_*, and *Candida _parapsilosis_*

*Candida _auris_* is an emerging fungal pathogen and is commonly _*resistant*_ to at least one class of antifungal drugs

*Mucor*, _*Rhizopus*_, _*Rhizomucor*_, _*Cunninghamella*_, and _*Absidia*_ are moulds and zygomycetes

*Aspergillus*, and _*Fusarium*_, are moulds but not zygomycetes

*Blastomyces*, _*Coccidiodes*_, _*Histoplasma*_, and _*Sporothrix*_ are dimorphic fungi

Name the generic name for each of the following brand names:

Diflucan = _*fluconazole*_ Sporanox = _*itraconazole*_ VFEND = _*voriconazole*_ Noxafil = _*posaconazole*_

Cresemba = _*isavuconazole*_ Mycamine = _*micafungin*_ Eraxis = _*anidulafungin*_ Cancidas = _*caspofungin*_

Abelcet = _*amphotericin B lipid*_ Fungizone = _*amphotericin B conventional/deoxycholate*_ Ambisome = _*amphotericin B liposomal*_

Azoles work by interfering with _*ergosterol*_ synthesis, which is the principal _*sterol*_ in the fungal _*fungal cell wall*_

*Fluconazole* (and many other azoles) is _*fungistatic*_ versus most yeasts (*e.g.*, Candida species) and _*fungicidal*_ versus many moulds

*Candida _glabrata_* can be susceptible dose-dependent (SDD) tor resistant to fluconazole

*Candida _krusei_* is intrinsically resistant to fluconazole

*Voriconazole* is generally considered the drug of choice for treating Aspergillus species

Echinocandins work by _ *inhibiting 1,3-beta-D-glucan synthesis* _, a component of the fungal _*cell wall*_

Echinocandins exhibit _*fungicidal*_ activity versus many Candida species

Polyenes work by binding to _*ergosterol*_ and altering fungal _*fungal cell membrane permeability*_ leading to leakage of cell components and fungal cell death

Polyenes are generally _*fungicidal*_ antifungals

Most azoles have excellent _*bioavailability*_ and are good candidates for IV to PO programs. Echinocandins are only available _*IV*_.

Azole antifungals are notorious for drug-drug interactions as _*inhibitors*_ or _*substrates*_ of CYP-450, beware elevation of _*liver enzymes*_ from azoles

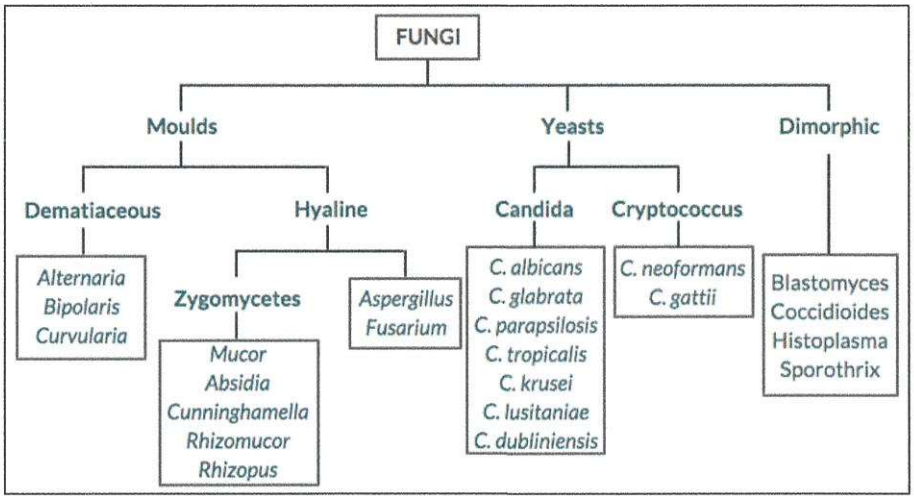
Polyene toxicities of utmost importance include _*nephrotoxicity*_, _*hypomagnesemia*_, _*hypokalemia*_, *and* _*infusion-mediated reactions*_

Conventional amphotericin B is associated with more _*nephrotoxicity*_ than amphotericin B lipid or liposomal

Therapeutic drug monitoring is commonly employed for _*posaconazole*_ (typical goal range _> 0.7_) and _*voriconazole*_ (typical goal range _*1 to 5*_)

Antifungals Cheat Sheet

Generalized Antifungal Spectrum of Activity							
Organism	Polyenes	Azoles					Echinocandins
	Ampho B	Flu	Itra	Vori	Posa	Isavu	Mica/Anidula/Caspo
Aspergillus sp.	+/-	-	+	+	+	+	+
Candida albicans	+	+	+	+	+	+	+
Candida glabrata (*Nakaseomyces glabrataa*)	+	+/-	+/-	+	+	+	+
Candida krusei (*Pichia kudriavzevii*)	+	-	+/-	+	+	+	+
Candida lusitaniae (*Clavispora lusitaniae*)	-	+	+	+	+	+	+
Candida parapsilosis	+	+	+	+	+	+	+/-
Cryptococcus neoformans	+	+	+	+	+	+	-
Coccidiodes spp.	+	+	+	+	+	+	-
Blastomyces	+	+	+	+	+	+	-
Histoplasma spp.	+	+	+	+	+	+	-
Fusarium spp.	+/-	-	-	+/-	+/-	+/-	-
Zygomycetes	+/-	-	-	-	+	+	-



Class	Mechanism
Polyenes	Binds to ergosterol, disrupts cell membrane permeability
Azoles	Interferes with ergosterol synthesis
Echinocandins	Inhibits 1,3-beta-D-glucan synthesis

Potential Amphotericin B Pre-Medications
Acetaminophen
NSAID
Hydrocortisone
Diphenhydramine
Meperidine (PRN rigors)
NS / hydration

Drug	Brand Name(s)	IV	PO
Amphotericn B	Fungizone (conventional) Abelcet (lipid) Ambisome (liposomal)	✓	No
Ketoconazole	-	No	✓
Fluconazole	Diflucan	✓	✓
Itraconazole	Sporanox	✓	✓
Voriconazole	VFEND	✓	✓
Posaconazole	Noxafil	✓	✓
Isavuconazole	Cresemba	✓	✓
Micafungin	Mycamine	✓	No
Anidulafungin	Eraxis	✓	No
Caspofungin	Cancidas	✓	No

Drug	Goal Level	When To Monitor
Itraconazole	0.5 - 1	4-7 days after starting
Posaconazole	> 0.7	≥ 7 days of therapy
Voriconazole	1 - 5	≥ 5 days of therapy

Drug/Class	Beware…
Azoles	Hepatotoxicity, QT prolongation, drug-drug interactions
-Voriconazole	Hallucinations & visual disturbances w/ high levels
-Itraconazole	Boxed warning with heart failure
Polyenes	Nephrotoxicity, infusion reactions (less with Abelcet and Ambisome), hypo-K, hypo-Mg

- Azoles are inhibitors of CYP-450, so they will INCREASE levels of other drugs metabolized by this pathway
  - Beware contraindications due to drug-drug interactions and Azole antifungals
- Voriconazole is generally considered the go-to drug for *Aspergillus* sp. infections
- Echinocandins do not penetrate the CSF or the urine, do not use them for meningitis or UTI
- Conventional amphotericin B has more nephrotoxicity associated with it than the lipid or liposomal formulations

Abbreviations: Ampho B = Amphotericin B, Anidula = anidulafungin, Caspo = caspofungin, Flu = fluconazole, Isavu = isavuconazole, Itra = itraconazole, Mica = micafungin, Posa = posaconazole, Vori = voriconazole

Antifungal Drugs Rapid Fire Test

Question #1
List at least 3 antifungal drugs from the azole class.

Question #2
Name at least 2 antifungal drugs from the echinocandin class.

Question #3
What 3 formulations does the polyene antifungal drug amphotericin B come in?

Question #4
Which two classes of systemic antifungal drugs work through interfering with ergosterol synthesis?

Question #5
What is the mechanism of action of the echinocandins?

Question #6
Does fluconazole (Diflucan) require dose-adjustments for renal function?

Question #7
Which amphotericin B products are dosed using 3-10 mg/kg IV daily?

Question #8
Amphotericin B can be nephrotoxic, but does it require dose adjustment for renal function?

Question #9
What side effects earned amphotericin B the nickname "amphoterrible" amongst providers?

Question #10
What pre-medications may be useful in managing infusion-mediated reactions and side effects associated with amphotericin B?

Question #11
What is the difference in regards to side effects of the different amphotericin B products?

Question #12
Which echinocandin does not require a loading dose?

Question #13
Which antifungal drug is generally considered the drug of choice for Aspergillus infections?

Question #14
Which Azole antifungal is a go-to for fungal infections caused by zygomycetes?

Question #15
Which Candida species is inherently resistant to fluconazole?

Question #16
Which yeast can either be susceptible dose-dependent or resistant to fluconazole?

Question #17
When an Azole antifungal cannot be used to treat Candida spp. in the blood (candidemia), what drug class is typically employed?

Question #18
What yeast is known to cause meningitis in HIV+ patients?

Question #19
Induction therapy for cryptococcal meningitis is typically done with what drug(s)?

Question #20
Following induction therapy with flucytosine + amphotericin B for cryptococcal meningitis, is consolidation therapy necessary?

Question #21
Do echinocandins have a role for treatment of meningitis?

Question #22
Which antifungal agent is sometimes administered by the intrathecal route for meningitis?

Question #23
What are the 3 major endemic fungi and where are they endemic to in the United States?

Question #24
What class of antifungals is associated with drug-drug interactions via inhibition of CYP-450 enzymes?

Question #25
What is the percent oral bioavailability of fluconazole (Diflucan), voriconazole (VFEND), and isavuconazole (Cresemba) in adults?

Question #26
What has a more reliable pharmacokinetic profile, posaconazole solution or posaconazole delayed-release tablets?

Question #27
Itraconazole (Sporanox) should not be used in patients with what comorbidity?

Question #28
What is the typical goal trough level for voriconazole?

Question #29
What is the typical goal level range for patients on posaconazole?

Question #30
What toxicity is of particular concern with oral ketoconazole?

Question #31
What type of cardiac toxicity is associated with the azole antifungals?

ANSWERS

Question #1 answer: 1. Ketoconazole 2. Itraconazole (Sporanox) 3. Fluconazole (Diflucan) 4. Voriconazole (VFEND) 5. Posaconazole (Noxafil) 6. Isavuconazole (Cresemba)

Question #2 answer: 1. Micafungin (Mycamine) 2. Anidulafungin (Eraxis) 3. Caspofungin (Cancidas)

Question #3 answer: 1. Conventional amphotericin B (Fungizone) 2. Amphotericin B lipid complex (ABLC, Abelcet) 3. Liposomal amphotericin B (L-amb, Ambisome)

Question #4 answer: 1. Polyenes (bind to ergosterol and alters membrane permeability) 2. Azoles (inhibit ergosterol formation)

Question #5 answer: Inhibition of 1,3-beta-D-glucan synthesis, leading to reduced cell wall stability and cellular lysis

Question #6 answer: Yes

Question #7 answer: 1. Amphotericin B lipid complex (Abelcet) 2. Liposomal amphotericin B (Ambisome)
(Conventional amphotericin B is dosed 0.7-1.5 mg/kg IV daily)

Question #8 answer: No renal dose adjustments required

Question #9 answer: Infusion-mediated reactions (fever, chills, rigors, hypotension, hypertension, flushing, thrombophlebitis, etc)

Question #10 answer: Acetaminophen (Tylenol), diphenhydramine (Benadryl), NSAIDs, methylprednisolone (Methylpred), meperidine (Demerol, for rigors), fluids (NS)

Question #11 answer: Nephrotoxicity: conventional >>> lipid = liposomal Infusion reactions: conventional >>> lipid > liposomal
[Note 1: this is a debated topic]
[Note 2: meperidine (Demerol) is a common drug to use if rigors occur]

Question #12 answer: Micafungin (Mycamine)

Question #13 answer: Voriconazole (VFEND)

Question #14 answer: Posaconazole (Noxafil)

Question #15 answer: *Candida krusei*

Question #16 answer: *Candida glabrata*

Question #17 answer: An echinocandin

Question #18 answer: *Cryptococcus neoformans*

Question #19 answer: Amphotericin B + flucytosine

Question #20 answer: Yes. This is usually done with fluconazole.

Question #21 answer: No. They do not enter the CNS.

Question #22 answer: Amphotericin B (particularly for coccidioidal meningitis)

Question #23 answer: (1) *Blastomyces dermatitidis* - Ohio & Mississippi River Valleys and the Great Lakes (2) *Histoplasma capsulatum* - Ohio & Mississippi River Valleys (3) *Coccidioides immitis* - Southwestern United States (e.g., Arizona, New Mexico)

Question #24 answer: Azoles (as inhibitors, they increase the concentrations of other drugs [e.g., phenytoin]. As substrates, other drugs can effect their concentration [e.g., rifampin decreases systemic azole concentrations])

Question #25 answer: >90%, making them excellent targets for IV to PO programs

Question #26 answer: Delayed-released tablets have more reliable absorption. There is a delayed-released oral suspension that came out in 2021, but that may not be in widespread use. This question is directed towards the older solution having less reliable absorption.

Question #27 answer: Heart failure

Question #28 answer: 1-5 mg/L (beware toxicity like ocular effects with levels >5 mg/L)

Question #29 answer: >0.7 mg/L (absorption can be hard to predict and many clinicians start by shooting for "at least detectable")

Question #30 answer: Hepatotoxicity. Beware hepatotoxicity with all azole antifungals.

Question #31 answer: QTc prolongation and arrhythmias / torsades de pointes.

Antivirals Cheat Sheet

Drugs are categorized with viruses they are most commonly used for. They may have activity versus other viruses.

Influenza Drugs				
	Oseltamivir	**Zanamivir**	**Peramivir**	**Baloxavir marboxil**
Brand name	Tamiflu	Relenza	Rapivab	Xofluza
FDA Approval	2000	1999	2014	2018
Class	Neuraminidase inhibitors			Polymerase acidic endonuclease inhibitor
Generic available	Yes	No	No	No
Route	Oral	Inhaled	IV	Oral
Adult treatment dose	75mg Q12h x5 days	10mg Q12h x5 days	600mg x1	20-79kg: 40mg x1 80kg or more: 80mg x1
Adult prophylaxis dose	75mg Q24h x7-10 days	10mg Q24h x7 days	Not approved for prophylaxis	20-79kg: 40mg x1 80kg or more: 80mg x1
Renal adjust	CrCl < 60	No	CrCl < 50	No
Other notes	Beware nausea, vomiting, headache, diarrhea	Not recommended w/ asthma or COPD	Has cross-resistance with oseltamivir but not zanamivir	Concerning post-marketing reports of anaphylactic shock
Initiation of therapy	These medications work best when started within **48 hours** of symptom onset (treatment) or exposure (prophylaxis with oseltamivir or zanamivir or baloxavir)			

Herpes Simplex Virus 1, Herpes Simplex Virus 2, and Herpes Zoster Virus Drugs			
	Acyclovir	**Valacyclovir**	**Famciclovir**
Brand name	Zovirax	Valtrex	Famvir
Generic available	Yes	Yes	Yes
Route	Oral, IV, topical	Oral	Oral
Usual frequency	3-5 doses per day	1-3 doses per day	2-3 doses per day
Renal adjust	CrCl < 50	CrCl < 50	CrCl < 60
Other notes	Beware crystaluria with high-dose IV; Dose using adjusted body weight in obesity	Less frequent dosing means better adherence	Tablets not recommended for patients with galactose intolerance
Mechanism of action	Valacyclovir is the prodrug of acyclovir. It is converted to acyclovir by intestinal and hepatic metabolism. Acyclovir converts to a monophosphate then a triphosphate form, which inhibits viral replication and DNA synthesis Famciclovir is converted to the prodrug penciclovir. Penciclovir converts to a monophosphate form, then a triphosphate form, which interferes with viral DNA replication and synthesis.		

- Be careful not to confuse valacyclovir (Valtrex) with valganciclovir (Valcyte)
- Initiate herpes simplex therapy as soon as possible in relation to onset of symptoms (*e.g.*, tingling sensation)
- To try to prevent crystaluria many providers give maintenance NS + bolus NS pre-dose / post-dose with IV acyclovir

Cytomegalovirus (CMV) Drugs						
	Ganciclovir	**Valganciclovir**	**Foscarnet**	**Cidofovir**	**Letermovir**	**Maribavir**
Brand	Cytovene	Valcyte	Foscavir	Vistide	Prevymis	Livtencity
Route	Oral, IV, Ophth	Oral	IV	IV	Oral, IV	Oral
Renal dose	CrCl < 70	CrCl < 60	Yes, it's complicated	Avoid if CrCl ≤ 55	Caution w/ CrCl < 50	No
Nephrotoxicity	+	+	+++	+++	-	-
FDA Boxed Warnings	Hematologic toxicity, teratogenic/ carcinogenic	Hematologic toxicity, teratogenic/ carcinogenic	Nephrotoxicity, seizures	Nephrotoxicity, neutropenia, teratogenic/ carcinogenic	None	None, but beware drug interactions via CYP3A4
Mechanism of action	Inhibits viral DNA synthesis	Converts to ganciclovir	Inhibits viral DNA polymerase	Interferes with the growing viral DNA chain	Targets CMV DNA terminase required for viral processing and packaging	Inhibits protein kinase of enzyme pUL97

- The UL97 and UL54 genes confer ganciclovir resistance. UL54 can also cause cidofovir and foscarnet resistance. Letermovir was FDA-approved in November 2017 for CMV prophylaxis, so clinical experience is a bit limited, but it may have less side effects than the other CMV drugs and it does not have cross-resistance with the other CMV drugs.
- Ganciclovir oral is rarely used and the IV formulation requires preparation in a vertical flow-hood.
- Ganciclovir and valganciclovir doses are higher with induction therapy as compared to maintenance therapy.

Abbreviations: CMV = cytomegalovirus, CrCl = creatinine clearance, FDA = Food and Drug Administration, IV = intravenous, NS = normal saline

Biostatistics Cheat Sheet

Summary of Data Types				
	Nominal	Ordinal	Continuous	
			Interval	Ratio
Definition:	Data without order or indication of relative severity	Data ranked in a specific order but without a consistent magnitude	Data ranked in a specific order that includes a constant difference in magnitude of change. Zero is arbitrary	Data ranked in a specific order that includes a constant difference in magnitude of change. Zero is NOT arbitrary.
Examples:	Sex, mortality	Trauma score	Temperature	Blood pressure, heart rate
Eligible for parametric tests:	No	No	If normally distributed	
Typical measure of central tendency:	Not applicable	Median	Mean / average	

EQUATIONS

	Outcome Yes	Outcome No
Intervention	Group A	Group B
Control	Group C	Group D

Intervention event rate = A/B Control event rate = C/D

OR = (A/C) / (B/D) or (AD/BC) RR = A/(A+B) / C/(C+D) RRR = 1 – RR

ARR = A/(A+B) – C/(C+D) NNT = 1/ARR Power = 1 – β

Think of type 1 and type 2 errors like the boy who cried wolf, who made both in that order: First everyone believed there was a wolf when there was not. Then they believed there was no wolf when there was one. Just replace the word "wolf" with the word "effect."

If the...	...it will...
Sample size decreases	Make the study require less resources to perform
Sample size increases	Increased the power
Power increases	Make results more reliable
Confidence interval narrows	Reduce uncertainty
P-value gets smaller	Reduce likelihood outcomes occurred by chance
Standard deviation gets smaller	Imply reduced variability in the sample
Data is not normally distributed	Not allow for parametric tests to be used
Odds ratio is < 1	Make the outcome less likely in the intervention group
Relative risk is < 1	Suggest a negative association between the intervention & outcome
ARR becomes less	Mean the intervention is less meaningful
Alpha increases	Increase the chance of a type I error
Beta increases	Increase the chance of a type II error
Study has extreme outliers	Not impact the median as much as it would impact the mean

When the...	...it means...
Data being produced by a project is intended to contribute to generalizable knowledge	It is a research project
Study poses any threat to human subjects	Institutional review board approval is required
Conclusion is that there is a difference when there actually is no difference	A type I error has occurred
Conclusion is that there is no difference when there actually is a difference	A type II error has occurred
Subject remembers an event differently from how it occurred	There is recall bias
Study subjects alter their behavior due to awareness of being in a study	The Hawthorne Effect is occurring
Study design is not consistent with standard clinical practices	The study has limited external validity
Study is observational in design	There is no intervention group
Study is a snapshot of a population at one point in time	It is a cross-sectional study
Design is a case-control study	It is an observational study
Use of multivariate logistical regression is employed	Independent variables can be identified

Abbreviations: ARR = absolute risk reduction, NNT = number needed to treat, OR = odds ratio, RR = relative risk, RRR = relative risk ratio

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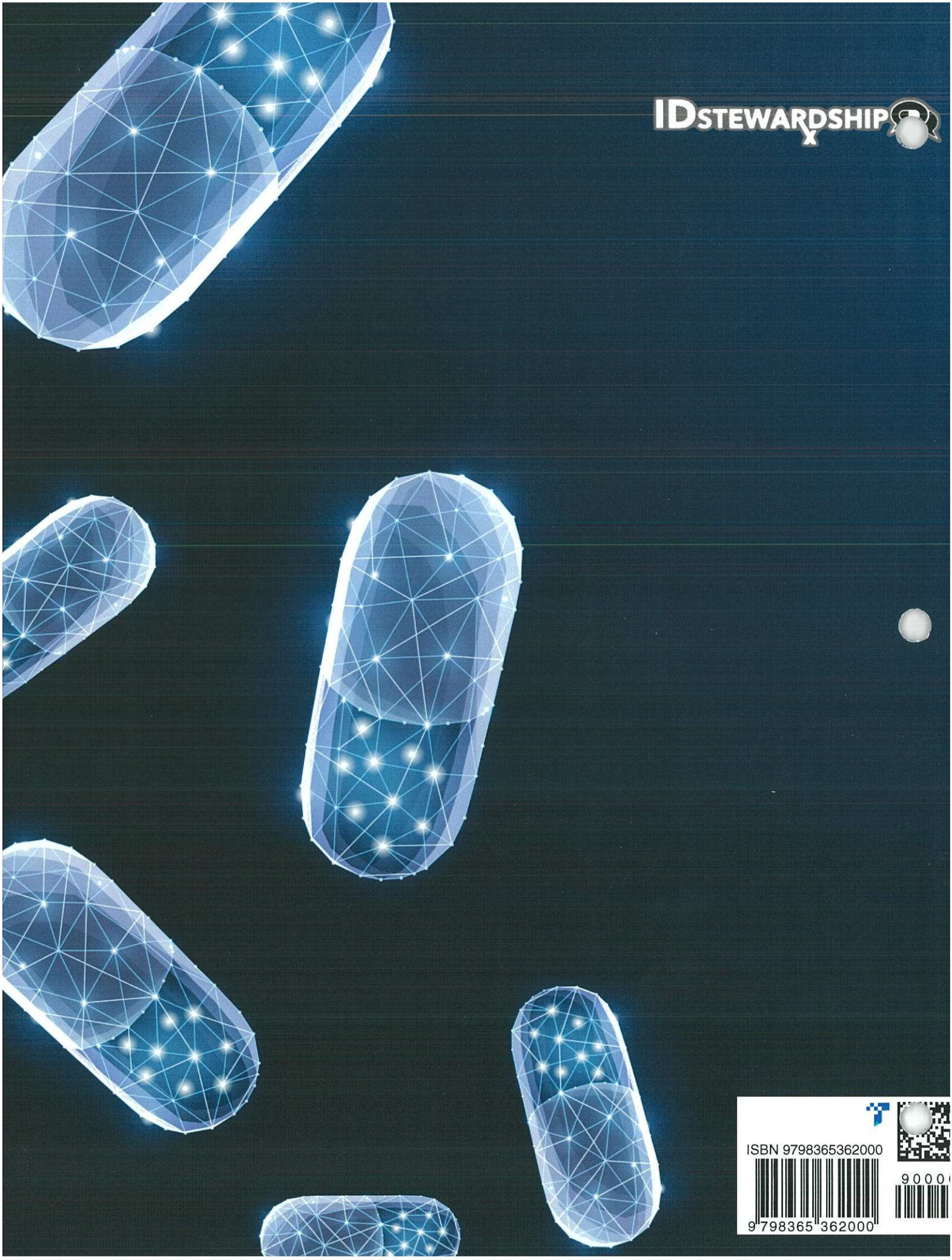

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